Ceria-supported Ruthenium Catalysts Directed toward Greener Organic Reactions(Dissertation_全文)

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General Introduction

1. Background

1-1. Introduction

In the 21st century, sustainable human progress has been recognized as a high priority worldwide. With regard to this issue, Anastas and Warner developed 12 principles of green chemistry in 1998 [1], which prompted chemists to focus on the development of environmentally-benign processes for synthesizing organic compounds [2]. Particularly, the further development and improvement of catalysts that can make it possible to reduce the environmental load are regarded as the most important issues in the field of industrial chemistry [3].

Catalysts can be divided broadly into two categories: “homogeneous catalysts” and “heterogeneous catalysts”. The former are defined as catalysts that exist in the same phase as the substrates and products, and most are in a liquid phase. Inorganic lquid acid or base catalysts, metal-complex catalysts, organocatalysts and enzymes are representative examples of homogeneous catalysts. In contrast, heterogeneous catalysts are defined as catalysts that exist in a different phase from the products. Solid acid or base catalysts, supported metal catalysts and immobilized metal-complex catalysts are representative heterogeneous catalysts.

Transition-metal complex catalysts are some of the most promising homogeneous catalysts [4]. Ligands and external additives can create precisely controlled active metal species, which can realize highly efficient organic transformations with high selectivity

under relatively mild reaction conditions. The remarkable progress with homogeneous complex catalysts in the 20th century revolutionized synthetic chemistry, and many chemists who studied homogeneous complex catalysts received the Nobel Prize for their work. For example, the prizewinners in 2010, A. Suzuki, E. Negishi and R. Heck, developed homogeneous Pd-catalyzed cross-coupling reactions, which had a strong impact on synthetic chemistry [5]. However, homogeneous catalysts have some inherent disadvantages, such as the difficulty of recovering and recycling the catalysts after the reaction. Thus, only a few processes are used in industry so far.

In contrast, heterogeneous catalysts can overcome these problems. They can be easily recovered from the reaction mixture without severe contamination of the products by metallic species, and can be easily reused or recycled. Thus, from the viewpoint of green and sustainable chemistry, much attention has been focused on synthetic processes with heterogeneous catalysts [6].

1-2. Heterogeneous catalysts for selective organic transformations

In the field of heterogeneous catalysts, the development of metal complex catalysts immobilized on solid supports as well as solid-supported metal catalysts are major research targets. The following sections describe the features of these two categories.

1-2-1. Immobilized metal-complex catalysts

Immobilized metal-complex catalysts can be defined as catalysts in which a metal-complex is tethered to a solid support or polymer through stable chemical bonds. They can be easily separated from the reaction mixture and can be reused after the reactions. Due to their regulated structure around the active site with ligands, they are

expected to show catalytic activities and selectivities comparable to those of homogeneous metal-complex catalysts. For example, Jacobsen et al. reported the synthesis of chiral Co-salen complexes tethered to a polymer, which showed high catalytic activity for the kinetic resolution of epoxides without any decrease in stereoselectivity compared to those of homogeneous catalysts [7]. Furthermore, a flow system with silica-immobilized Co catalysts has been developed [8].

Steric restriction around active sites by the support can induce unexpected catalytic functions that are difficult to achieve with homogeneous catalysis. For instance, Tada et al. reported that the immobilization of a Ru(II) complex on a silica support greatly improved its catalytic activity for the epoxidation of *trans*-stilbene [9]. Immobilization on the support is thought to stabilize very unstable active Ru species with O_2 side-on coordination.

Immobilization of complex catalysts could boost their stereoselectivities [10]. A chiral Rh-complex catalyst immobilized inside the pores of mesoporous silica, MCM-41, realized a highly efficient enantioselective hydrogenation of methyl benzoylformate, whereas the parent Rh complex showed no stereoselectivity [11].

Complex catalysts that are directly bound to the surfaces of metal oxide supports also act as heterogeneous catalysts for organic transformations [12]. Basset, Copéret and co-workers focused on the construction of well-defined organometallic species on the surface of metal oxides and studied on their use as heterogeneous catalysts: This strategy is known as “Surface Organometallic Chemistry (SOMC)” [13]. For example, in 1991, they reported the synthesis of d^0 surface Zr complexes on SiO_2 [14], which are transformed to a Zr-H complex by the reaction with H_2 at 150 ^oC [15]. Furthermore, such surface metal hydride species have been shown to catalyze the disproportionation of

neopentane to methane and isobutene via a "σ-bond metathesis pathway" [16]. Recent remarkable progress in spectroscopic analysis has greatly contributed to the further development of SOMC: The detailed structure of a Zr-H complex has been determined by using X-ray absorption fine structure (XAFS) analysis and solid-state NMR. Recently, dynamic changes in the surface complex have also been investigated on the basis of in situ and/or time-resolved spectroscopic measurements. These novel techniques facilitate the precise construction of highly active catalytic sites on the solid surface [12]. In this context, the fine structure of Re species of $MeReO_3/Al_2O_3$ as well as the mechanism for the generation of active Re species for olefin metathesis was proposed by making full use of various spectroscopic analyses and a theoretical study [17].

As discussed above, immobilized catalysts are advantageous in terms of their high activities and selectivities for various organic reactions, and they often show unexpected catalytic functions that are not seen with homogeneous catalysts. However, there are still several intrinsic problems associated with their practical application, such as the cumbersome operations required for their preparation, their low chemical stabilities, and so on.

1-2-2. Supported metal catalysts

Supported metal catalysts are generally considered to be catalysts in which metal particles are dispersed on insoluble solid supports such as metal oxides or activated charcoal. Their higher stabilities simplify their preparation and operation in comparison with immobilized metal-complex catalysts. The state and nature of the surface metallic species are critically influenced by the support, and a particular combination of metallic species with a support can create specific supported metallic species, which could show

unexpected catalytic features [18].

Kaneda et al. reported the synthesis and catalytic properties of Ru catalysts supported on hydroxyapatite (HAP) by the treatment of $RuCl_3$ *n*-hydrate with HAP in water [19]. The supported Ru catalysts participated in various organic transformations, such as the oxidation of alcohols with molecular oxygen [19], the oxidation of amines to nitriles [20], the hydration of nitriles [21] and the oxidation of silanes to silanols [21]. Successful reuse of the catalysts was demonstrated and the leaching of Ru species into the reaction mixture is negligible. The formation of isolated 5-coordinated Ru(III)-Cl species on HAP has been proposed on the basis of a detailed XAFS study. Furthermore, treatment of the catalysts with silver(I) triflate transformed the Ru(III) species supported on HAP into cationic Ru species, which functioned as a heterogeneous Lewis acid catalyst for Diels-Alder reactions and aldol-type condensations with high efficiency [22].

Ruthenium catalysts supported on hydrotalcite (HT), which is a clay mineral with a layered structure, were found to be effective for the α-alkylation of nitriles with alcohols [23]. Ru species acted as a dehydrogenation catalyst for alcohols and HT acted as a base catalyst, and the combination of these functionalities has been proposed to be essential for the catalysis. An XAFS study suggested the formation of isolated Ru(IV)-OH species coordinated by two H_2O molecules on the surface of HT.

Such Ru-OH species could be constructed on the surface of various metal oxide supports by a simple impregnation method [24]. Mizuno and co-workers reported the $Ru(OH)_x/Al_2O_3$-catalyzed selective synthesis of nitriles from alcohol with NH_3 [25]. The solid catalysts showed higher activities than previously reported homogeneous Ru complex catalysts, Ru/C or Ru/HAP catalysts. Moreover, $Rh(OH)_x/Al_2O_3$ prepared by a similar method as $Ru(OH)_x/Al_2O_3$ functioned as a very effective catalyst for the one-pot

synthesis of primary-amides from aldehydes with hydroxylamine [26]. Despite very low selectivities in classical acid-catalyzed reactions [27], the supported Rh catalysts gave the products with excellent selectivities.

The development of supported metal catalysts that are effective for carbon−carbon bond-forming reactions, such as Suzuki−Miyaura coupling, with supported metal catalysts has also been extensively studied, especially in the past decade [28]. For example, perovskite-type $LaFe_{0.57}Co_{0.38}Pd_{0.05}O_3$, which is well known as an effective catalyst for automobile emission control, a so-called "intelligent catalyst" [29], showed high activities for Suzuki−Miyaura coupling to achieve a high turnover number (TON) of over 200,000 [30]. Okumura et al. reported the formation of atomic Pd species encapsulated in a cage of USY zeolite and their excellent activity for Suzuki–Miyaura coupling. The USY zeolite-supported Pd catalysts were reported to show a much higher TON (over 10,000,000) than conventional Pd/C, Pd/Al_2O_3 and homogeneous $Pd(OAc)_2$ catalysts [31].

As mentioned above, recent improvements in supported metal catalysts have realized various organic transformations, including those that have been considered to be difficult even with the use of homogeneous metal-complex catalysts. However, there are still several problems. For example, the scope of the reactions with supported catalysts is rather limited to specific types, such as oxidation, hydrogenation and acid- or base-mediated reactions, probably because of the difficulty of fine-tuning the electronic and steric state of the active metal species. Thus, the application of supported metal catalysts for highly selective organic reactions such as C–C bond-formations via the activation of C–H or C–C bonds, remains a challenge in synthetic chemistry.

1-2-3. Ceria-supported Ru catalysts

In current catalyst chemistry, ceria (CeO_2) has drawn much attention as an attractive catalyst or catalyst support due to its high oxygen-storage capacity and metal-dispersion ability [18b,32]. CeO_2-supported noble-metal catalysts have been reported to show excellent activities for various reactions, such as the hydrogenation or oxidation of CO [33], the reduction of nitrogen oxides [34] and the combustion of hydrocarbons [35]. In particular, CeO_2-supported Ru catalysts (Ru/CeO_2) are known to be effective for the combustion of hydrocarbons [36], the synthesis of ammonia [37] and the wet oxidation of waste water [38]. In organic synthetic reactions, the selective oxidation of alcohols to the corresponding aldehydes and ketones has been achieved in the presence of Ru/CeO_2 [39] and $RuCo/CeO_2$ catalysts [40], whereas there have been no previous examples of the application of the Ru/CeO_2 catalysts to other types of organic transformations, such as C–C bond-forming reactions.

2. Scope and outline of the present thesis

Based on above background, this thesis focuses on the development of novel solid catalytic systems for highly selective organic syntheses in a green manner. In particular, ceria- or zirconia-supported Ru catalysts have been found to be very effective for various C–C or C–O bond-forming reactions, which have never been accomplished with other supported metal catalysts.

This thesis consists of eight chapters. Chapter 1 describes heterogeneous Ru-catalyzed sequential transfer-allylation and isomerization from tertiary homoallyl alcohols to aldehydes. Ru/CeO_2 and Ru/ZrO_2 showed activity for the reaction. In contrast,

Ru catalysts supported on SiO_2, Al_2O_3, TiO_2 or MgO were not effective at all. No additives such as phosphines, bases or CO are required, which facilitates the reuse of the catalysts without a significant loss of activity.

Chapter 2 describes the solid Ru catalysts for the direct arylation of aromatic C–H bonds with aryl halides. Ru/CeO_2 and Ru/ZrO_2 showed high activities for the reactions to give unsymmetrical biaryl compounds in high yields, even in the absence of phosphine ligands. Furthermore, reductive pretreatment of Ru/CeO_2 in the presence of PPh_3 under a hydrogen atmosphere markedly enhanced its catalytic activity, and the reaction with aryl chlorides proceeded efficiently to afford the products in excellent yields. A hot filtration test suggested that the solid Ru catalyst worked heterogeneously.

Chapter 3 reports the addition of aromatic C–H bonds to vinylsilanes in the presence of solid Ru catalysts. The reactions take place in the presence of Ru/CeO_2 or Ru/ZrO_2 catalysts together with PPh_3 to give the products in high yields. Moreover, Ru/CeO_2 catalysts that were pretreated together with PPh_3 under a hydrogen atmosphere showed very high activities and the reaction went to completion within a short reaction period at lower temperature.

Chapter 4 deals with further modification of the Ru/CeO_2 catalytic system for the addition of aromatic C–H bonds to alkenes (hydroarylation). The treatment of Ru/CeO_2 with PPh_3 and an aqueous solution of HCHO in 2-methoxyalcohol enhanced the catalytic activities and broadened the scope of substrates for hydroarylation. The solid Ru/CeO_2 could be recycled for several times after the reaction of unsaturated hydrocarbons.

Chapter 5 describes the addition of carboxylic acids to terminal alkynes by Ru catalysts supported on solid oxides. Ru/CeO_2 and Ru/ZrO_2 catalysts prepared from a Ru precursor with chloro ligands produced the corresponding vinyl esters in high yields. In

the present catalytic system, the *E*-isomers of anti-Markovnikov adducts were obtained as the major products.

Chapter 6 reports the regio- and stereo-selective production of vinyl esters via the addition of carboxylic acids to terminal alkynes by the use of Ru/CeO_2 catalysts. With the solid Ru/CeO_2 catalysts treated in the presence of 1,4-(bisdiphenylphosphino)butane (dppb) under a hydrogen atmosphere, the *Z*-isomers of anti-Markovnikov adducts were obtained in high yields with excellent selectivities. On the other hand, $P(^nOct)_3$-modified Ru/CeO_2 catalysts gave Markovnikov adducts as the major products.

Chapter 7 describes the intermolecular coupling of alkynes with acrylates by Ru catalysts supported on metal oxides. The reactions occurred in the presence of Ru/CeO_2 or Ru/ZrO_2 with a catalytic amount of sodium formate. The coupling of different alkenes was also realized. The results of a detailed spectroscopic analysis suggest the formation of distorted Ru(IV)-oxo species on the surface of the CeO_2 support, which were then transformed into catalytically active low-valent Ru species at the initial stage of the reaction.

Chapter 8 deals with the Ru-catalyzed intermolecular hydroacylation of alkynes. Ru/CeO_2 catalyst showed activity for the reaction in the presence of sodium formate and 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (Xantphos) to give the corresponding conjugated enones in moderate to high yields. Various aromatic aldehydes with or without coordinating groups could be used for the reactions. The solid Ru/CeO_2 catalysts could be recycled several times without a significant loss of activity.

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Chapter 1

A heterogeneous Ru/CeO_2 catalyst effective for transfer-allylation from homoallyl alcohols to aldehydes

1.1 Introduction

As discussed in the general introduction, the development of heterogeneous catalysts that show high catalytic activities and selectivities towards organic synthesis is of great significance from both industrial and environmental points of view [1–3]. Although recent progress on homogeneous catalysts has realized selective cleavage of carbon–carbon bonds under mild and neutral conditions [4], for example, transfer-allylation reactions [5,6], there is no reported example of solid oxide catalysts that are effective for these carbon–carbon bond cleaving reactions.

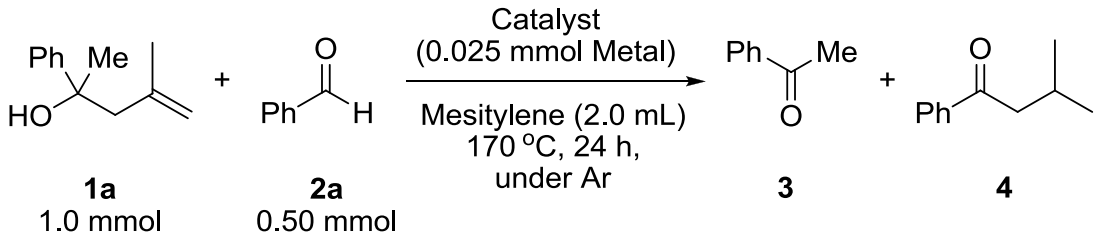
This chapter describes the heterogeneous Ru/CeO_2 catalyst [7] effective for transfer-allylation from homoallyl alcohols to aldehydes, followed by isomerization to give the corresponding saturated ketones in high yields, which proceeds *via* a different mechanism from that of Lewis acid-mediated reactions [8]. The present solid oxide-catalyzed reaction proceeds without additives such as phosphines, bases, and CO [5,6].

1.2 Results and discussion

The treatment of a homoallyl alcohol (**1a**) and benzaldehyde (**2a**) at 170 ^{o}C under an argon atmosphere in the presence of the Ru(2.0 wt%)/CeO_2 (0.025 mmol as Ru) gave saturated ketone **4a** in a good yield. As summarized in Table 1, the reaction was almost completed within 6 h (entries 3 and 4). No catalytic activity was observed below 150 ^{o}C (entry 5). The addition of phosphines to this Ru/CeO_2 catalyst completely suppressed the reaction, and no **4a** was obtained (entry 6). The reaction was sensitive to the molar ratio of homoallyl alcohols and aldehyde. The desired ketone, **4a**, was obtained in the best yield in the reaction of 0.50 mmol of **2a** with 1.0 mmol of **1a**. The effect of the catalyst support on the performance was examined. Among the supported Ru catalysts examined, only the Ru/CeO_2 catalyst showed the activity (entries 3, 7–10) [9]. As shown in entries 11–14, other transition metals supported on CeO_2 did not exhibit any catalytic activity either. Note that Lewis acidic TiO_2 (ST-01) [10] and/or Ru/TiO_2 catalyst gave 1,1,3-trimethyl-1*H*-indene, quantitatively, *via* the intramolecular Friedel-Crafts-type reaction of **1a** (entry 9). These results strongly suggested that the present transfer-allylation was not a carbonyl-ene reaction [8] promoted by acidic sites of the catalysts.

Under the present reaction conditions, the homogeneous $Ru_3(CO)_{12}$ catalyst gave **4a** in a lower yield than with the heterogeneous Ru/CeO_2 catalyst (entry 15). Note that $RuCl_2(PPh_3)_3$-catalyzed reaction under much more severe conditions afforded an $\alpha\beta$-unsaturated ketone, 3-methyl-1-phenylbut-2-en-1-one, in a low yield (entry 16) [5].

Table 1. Effect of solid oxide-supported catalysts on the transfer-allylation from **1a** to **2a**.



1a 1.0 mmol | **2a** 0.50 mmol | **3** | **4**

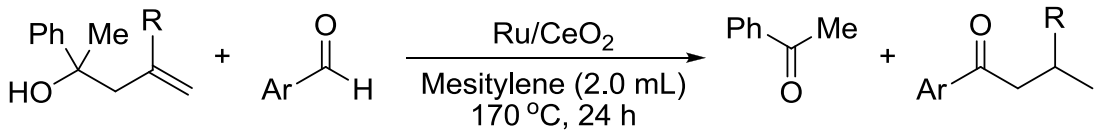
Entry	Catalyst[a]	Yield of **4a** (%)[b]
1	none	0
2	CeO_2	0
3	Ru/CeO_2	69
4[c]	Ru/CeO_2	63
5[d]	Ru/CeO_2	trace
6[e]	Ru/CeO_2	trace
7	Ru/SiO_2	0
8	Ru/Al_2O_3	0
9	Ru/TiO_2	0[f]
10	Ru/MgO	0
11	Fe/CeO_2	0
12	Cu/CeO_2	0
13	Rh/CeO_2	0
14	Pd/CeO_2	0
15	$Ru_3(CO)_{12}$[g]	15
16	$RuCl_2(PPh_3)_3$[g,h]	35[i]

[a] 2.0 wt%. [b] Determined by GLC based on **2a**. [c] Reaction time, 6 h.
[d] At 150 °C. [e] PPh_3 (0.10 mmol) was added. [f] 1,1,3-Trimethyl-*1H*-indene was obtained, quantitatively. [g] Homogeneous catalyst. [h] From ref. 5, **1a** (4.0 mmol), **2a** (4.0 mmol), Ru

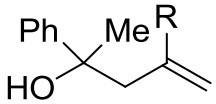
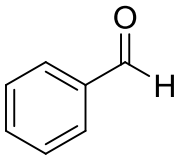
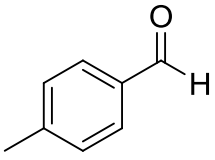
cat. (0.20 mmol), allyl acetate (30 mmol), THF (8.0 mL) under CO (10 atm) at 200 ^{o}C for 40 h. [i] The product was 3-methyl-1-phenylbut-2-en-1-one.

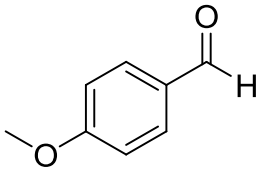
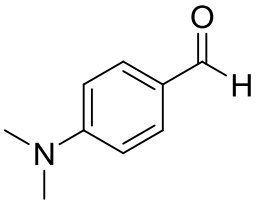
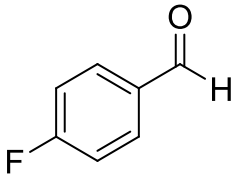
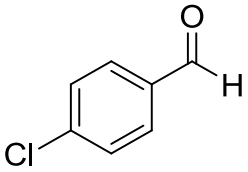
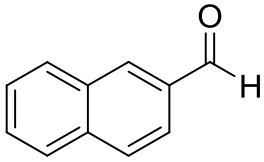
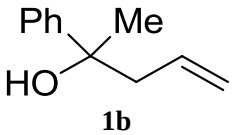
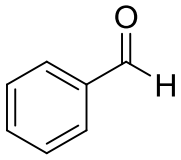
The results obtained by the Ru/CeO_2-catalyzed transfer-allylation–isomerization from a series of homoallyl alcohols with aldehydes under the optimized reaction conditions are shown in Table 2. The reaction of **1a** with aromatic aldehydes **2** proceeded smoothly to give desired ketones **4** in good to high yields. The substituents on the aromatic ring of **2** did not affect the reaction (entries 2–6), and 2-naphthaldehyde (**2g**) was also applicable (entry 7). Unexpectedly, the reaction of **1b** with benzaldehyde **2a** gave **4h** in a poor yield (entry 8). Aliphatic aldehydes, such as 1-octanal, gave a complex mixture due to the side reactions represented by an aldol condensation.

Table 2. Transfer-allylation from homoallyl alcohols (**1**) to aromatic aldehydes (**2**) catalyzed by Ru/CeO_2.[a]



1 **2** **3** **4**

Entry	**1**	**2**	Product	Yield of **4** (%)[b]
1	 **1a**	 **2a**	**4a**	69
2	**1a**	 **2b**	**4b**	78

3	**1a**	 **2c**		**4c**	93
4	**1a**	 **2d**		**4d**	(52)
5	**1a**	 **2e**		**4e**	64
6	**1a**	 **2f**		**4f**	(78)
7	**1a**	 **2g**		**4g**	(89)
8	 **1b**	 **2a**		**4h**	19

[a] *Reaction conditions:* **1** (1.0 mmol), **2** (0.50 mmol), mesitylene (2.0 mL), Ru/CeO_2 (0.025 mmol as Ru), at 170 °C for 24 h under Ar. [b] Determined by GLC based on **2**. Figures in the parentheses show isolated yields.

Figure 1 shows the time-course of the reaction of **1a** with **2a** catalyzed by Ru/CeO_2. During the initial stage of the reaction, the formation of secondary homoallyl alcohol **5a** was observed in GLC analysis. After 1.5 h of the reaction, with the decrease amount of **5a**, the formation of final product **4a** was observed. These results clearly reflect the sequential transfer-allylation and isomerization of an intermediate, **5a**.

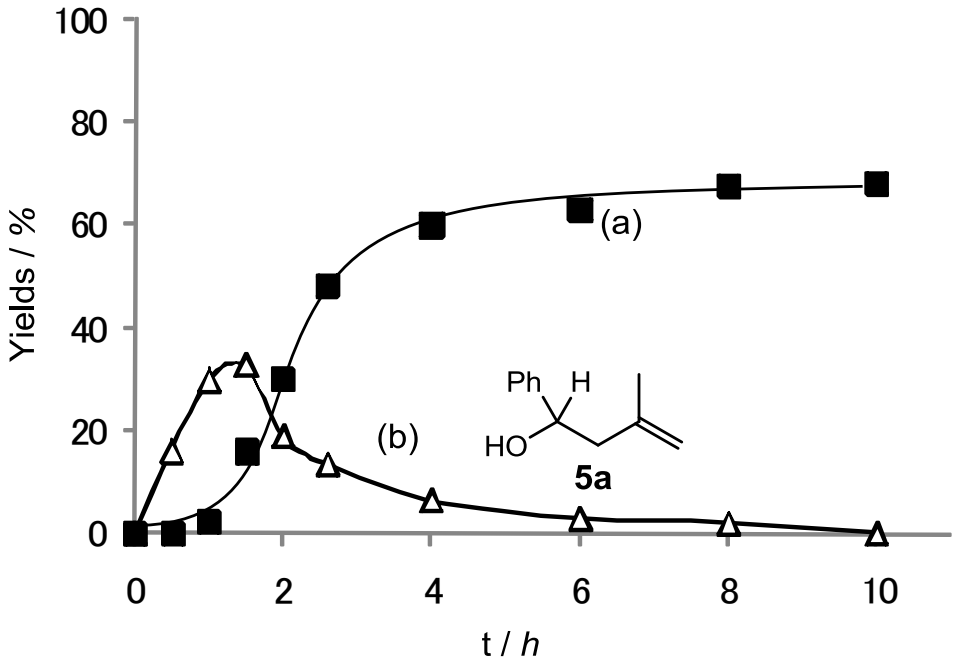
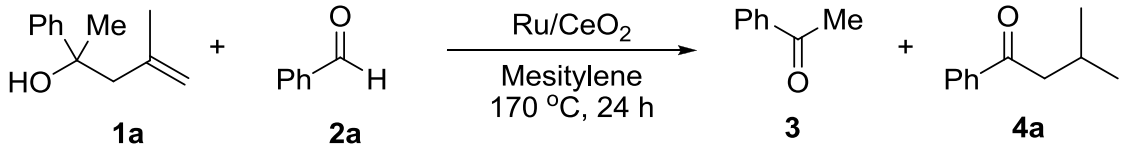


Figure 1. Time-course of the reaction of **1a** with **2a** during initial 10 h. (a) yield of **4a** (filled squares) and (b) yield of **5a** (see inset, open triangles). The reaction conditions were identical with those in Table 2.

One of the most advantageous points of heterogeneous catalysts is their high recyclability. The initial run was performed under the conditions shown in Table 3. After separation by the centrifugation, washing three times with diethyl ether (10 mL) at room temperature, and calcination at 400 ^{o}C for 30 min in air, the Ru/CeO_2 catalyst was reused for the reaction under the same conditions as for the initial run. Two series of the experiments were performed independently, and the results were shown in Table 3. These results clearly show that the Ru/CeO_2 catalyst was recyclable without a significant loss of activity. Note that reuse without calcination resulted in a poor yield of **4a** (less than 10% in the 2nd use), probably because of the significant deposition of a carbonaceous species on the catalyst surface.

Table 3. Activity of the recycled Ru/CeO_2 catalyst.[a]



Series	Catalyst	Yield of **4a** (%)[b]
1	1st use	69
	2nd use	68
2	1st use	61
	2nd use	59
	3rd use	62

[a] *Reaction conditions:* **1a** (2.0 mmol), **2a** (1.0 mmol), mesitylene (2.0 mL), Ru/CeO_2 (0.050 mmol as Ru), at 170 °C for 24 h under Ar.
[b] Determined by GLC based on **2a**.

It is important to investigate whether the reaction actually proceeds on the surface of the solid catalyst [11,12]. After the reaction of **1a** and **2a** at 170 ^{o}C for 24 h, the solid catalyst was removed by cold filtration. Subsequent addition of **1a** (1.0 mmol) and **2a** (0.50 mmol) to the clear filtrate, and heating of the mixture at 170 ^{o}C for an additional 24 h resulted in no increase of **4a**. ICP analysis revealed that the filtered solution contained only 0.0014 mmol of ruthenium species. Note that hot filtration of the solid catalyst after 3 h suppressed the further formation of the product **4a**. These results strongly suggest that the present catalytic reaction occurred on the solid surface, and that CeO_2 acts as a macro-ligand, which stabilizes the catalytically active ruthenium species.

The structure of the Ru/CeO_2 catalyst was investigated by spectroscopic analyses. The Ru(2.0 wt%)/CeO_2 catalyst shows typical type IV nitrogen adsorption/desorption isotherms (Figure 2), indicating that its pore size distributed in the mesopore region. The V-*t* plot analysis suggests the absence of micropores. The BET surface area of the Ru/CeO_2 catalyst was 92 m^2g^{-1}.

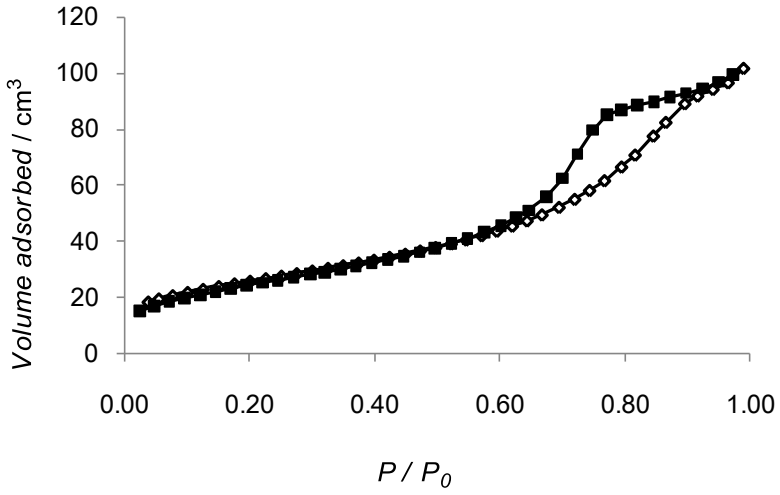


Figure 2. Nitrogen adsorption/desorption isotherms of the Ru(2.0 wt%)/CeO_2 catalyst. Open and filled marks stand for adsorption and desorption data, respectively.

Figure 3 shows the XRD patterns of the Ru/CeO_2 and Ru/TiO_2 catalysts, which only show broad diffraction peaks due to nanocrystalline cubic cerium oxide and anatase, respectively. The crystalline size of CeO_2 was estimated to be 11 nm by the Scherrer's equation from the 111 diffraction peak at 28^o. The absence of patterns corresponding to crystalline RuO_2 indicated the formation of well-dispersed ruthenium species.

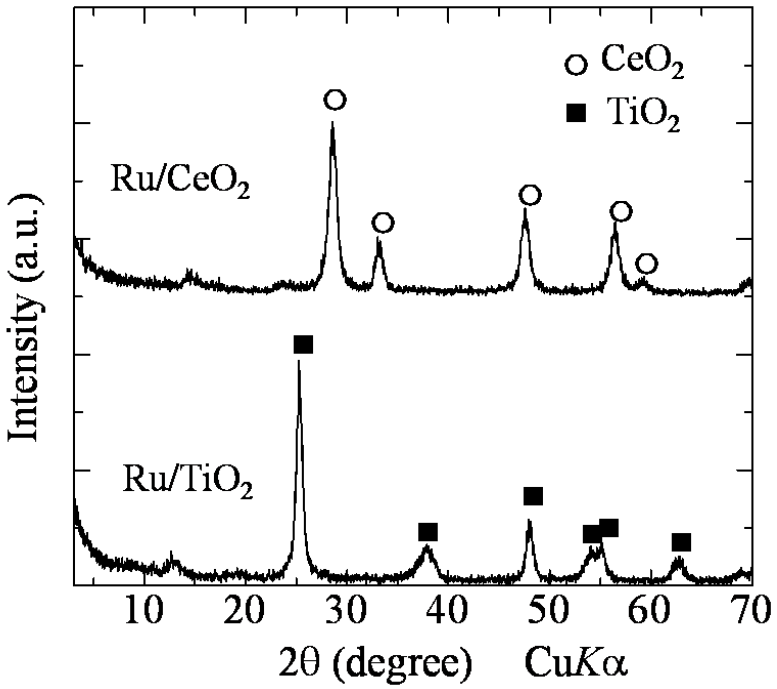


Figure 3. XRD patterns of the Ru(2.0 wt%)/CeO_2 and Ru(2.0 wt%)/TiO_2 catalysts.

The surface states of the catalyst before and after the catalytic run (Entry 3 in Table 1) were analyzed by XPS. Table 4 shows the surface composition and the binding energy of the Ru(2.0 wt%)/CeO_2 catalyst. The atomic ratio of carbon on the surface of the used catalyst was high, more than 18%, probably because of the deposition of carbonaceous materials on the surface during the catalytic run. A large part of carbonaceous species was removed by calcination at 400 ^oC for 30 min in air. The surface ratio of Ru was almost unchanged throughout the reaction and the subsequent calcination. Lower Ru $3d_{5/2}$ binding energy found in the used catalyst suggests the reduction of ruthenium(IV) species during the reaction.

Table 4. XPS analysis of the Ru(2.0 wt%)/CeO_2 catalyst.

Remarks	Surface concentration (atomic %)				Ru$3d_{5/2}$ (eV)
	C	Ru	Ce	O	
Before the reaction	11.87	1.01	30.28	56.84	280.4
After the reaction	18.38	1.08	30.63	49.90	279.2
After the 2nd reaction	11.07	1.08	29.52	58.32	280.6

The diffuse reflectance FTIR measurement of the Ru/CeO_2 catalyst showed a distinct band at 975 cm^{-1} that could be assigned to a ruthenium oxo species (Figure 4) [13]. Note that there were no signs of the Ru=O species for ruthenium catalysts supported on other carriers such as TiO_2. A previous XANES study revealed the presence of a five-coordinated ruthenium species in the Ru/CeO_2 catalyst prepared by a similar method [13].

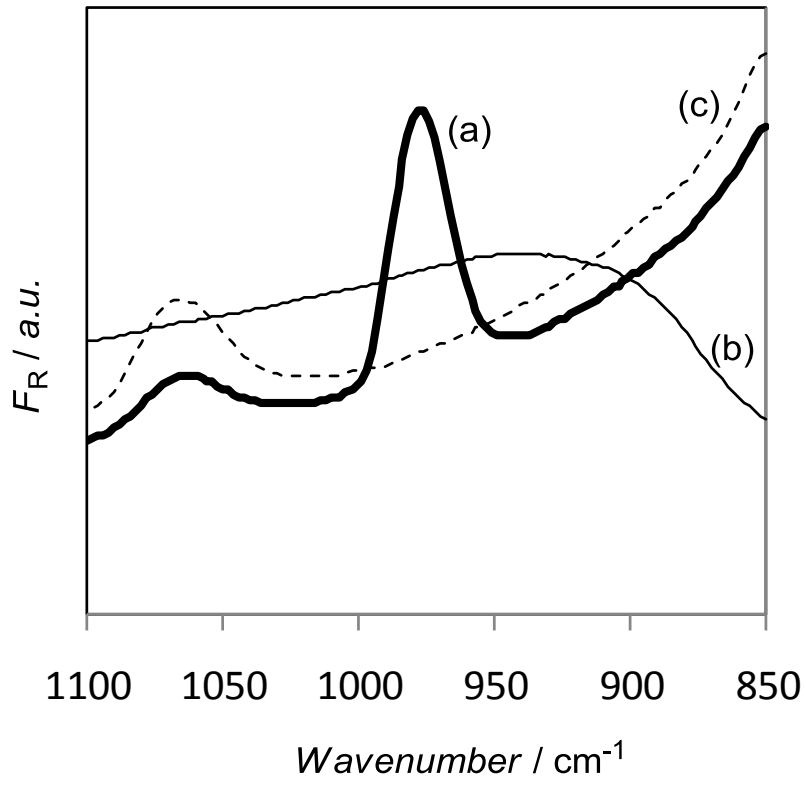


Figure 4. DRIFT spectra of the (a) Ru(2.0 wt%)/CeO_2 catalyst, (b) Ru(2.0 wt%)/TiO_2 catalyst, and (c) CeO_2.

A temperature-programmed reduction (TPR) measurement in a 1.9% H_2–Ar stream revealed that ruthenium species on CeO_2 were reduced at around 72 ^oC, which was lower than that in the reduction of bulk RuO_2 (*ca*. 105 ^oC) (Figure 5). These results supported an idea of the formation of a well-dispersed five-coordinated ruthenium(IV) oxo specie on the surface of Ru/CeO_2 [13], not on other supported Ru catalysts. Consequently, these oxo species would be reduced to form catalytically active low-valent ruthenium species on CeO_2.

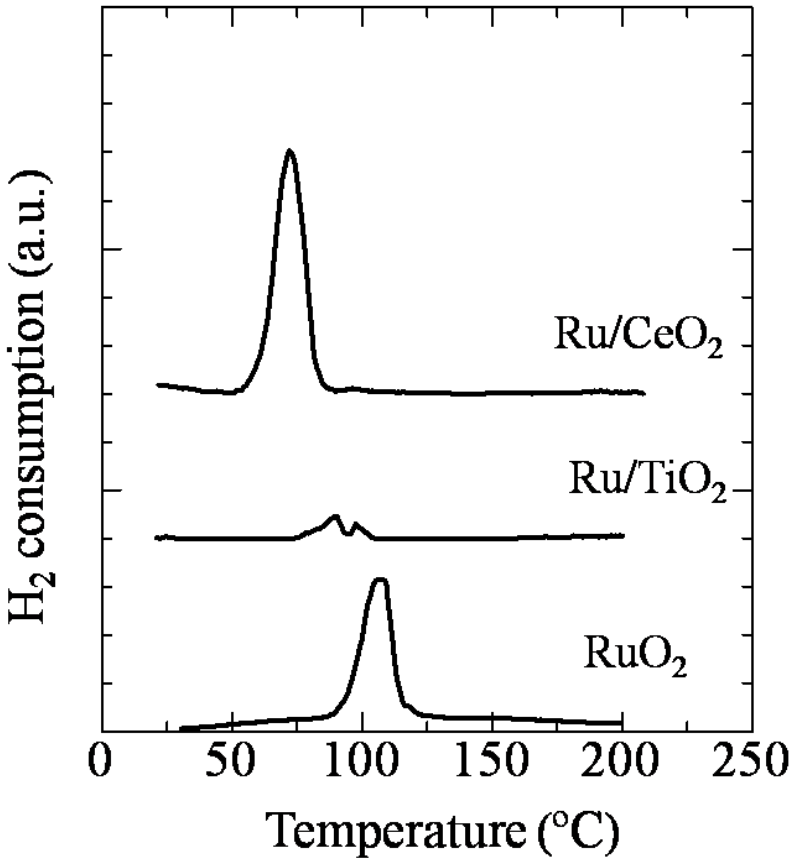


Figure 5. H_2 TPR profiles of the Ru(2.0 wt%)/CeO_2, the Ru(2.0 wt%)/TiO_2, and RuO_2.

Although the reaction mechanism is not clear yet, the initial step might consist of the oxidative addition of an OH group of **1** to an active ruthenium species. The following β-allyl elimination [5] would give **3** and an (allyl)ruthenium intermediate, which would react with an aldehyde to give the homoallyl alcohol (**5**). The formation of the stable allyl species on the surface of the Ru/CeO_2 catalyst has already been proposed on the basis of the spectroscopic study [13], when propene (C_3H_6) was treated by the Ru/CeO_2 catalyst.

1.3 Conclusions

In this chapter, the heterogeneous Ru/CeO_2-catalyzed sequential transfer-allylation–isomerization from homoallyl alcohols to aldehydes to give the saturated ketones is described. This simple solid oxide catalyst showed a comparable or superior performance to exquisite homogeneous transition-metal complex catalysts. No additives such as phosphines, bases, and CO were required, which facilitates reuse of the Ru/CeO_2 catalyst, and this feature is obviously attractive and advantageous from synthetic, industrial, and environmental perspectives.

1.4 Experimental

1.4.1 Materials and methods

All manipulations were performed under an argon atmosphere using standard Schlenk techniques. Homoallyl alcohols were prepared by the method reported in the literature [14]. Cerium oxide (CeO_2) was prepared by the treatment of a solution of cerium(III) nitrate hexahydrate (12.6 g, 29 mmol) in 400 mL of deionized water with 38 mL of 28% aqueous ammonia with stirring for 1 h at room temperature. The resulting precipitates were collected by centrifugation, and then died at 80 ^{o}C overnight. The product was heated in a box furnace at a rate of 10 ^{o}C min^{-1} and maintained at 400 ^{o}C for 30 min to afford CeO_2 in an excellent ceramic yield. Titanium oxide (ST-01), γ-alumina (JRC-ALO-8), silica (Cabosil), and MgO (Wako) were used as received. Ceria-supported Fe, Cu, Pd, and Rh catalysts were prepared by the impregnation method using iron(III) acetylacetonate, copper(II) acetate monohydrate, palladium(II) acetate, and tetrarhodiumdodecacarbonyl, respectively.

1.4.2 Characterizations

NMR spectra were recorded on a JEOL JNM-EX-400 (FT, 400 MHz (^{1}H), 100 MHz (^{13}C)) instrument. Chemical shifts (δ) are referenced to $SiMe_4$. Nitrogen adsorption/desorption isotherms were obtained with a computer-controlled automatic gas sorption system, Quantachrome NOVA 4200e. Samples were degassed at 300 ^{o}C for 2 h just before the measurements. The X-ray powder diffraction analyses (XRD: XD-D1, Shimadzu) were performed using Cu *K*α radiation and a carbon monochromator. The crystallite size of CeO_2 was calculated from the full width at half maximum (FWHM) of the 111 diffraction peak using Scherrer's equation. X-ray photoelectron spectra (XPS)

of the catalysts were acquired using an ULVAC-PHI 5500MT system equipped with a hemispherical energy analyzer using Mg *K*α radiation (15 kV, 400 W). Samples were mounted on indium foil and then transferred to an XPS analyzer chamber. Binding energies were referenced to the C 1s level of residual graphitic carbon [15]. Samples were sputtered for 1 min by an Xe^+ ion beam generated at 3.0 kV to remove carbonaceous contaminants. Diffuse reflectance IR spectra were recorded using a Nicolet Magna-IR 560 FT-IR spectrometer with DRIFT optical configuration. Temperature-programmed reduction (TPR) was carried out with a flow-type reactor. Hydrogen (1.9 vol.% in argon under atmospheric pressure at 30 mL min^{-1}) was passed through a reaction tube containing 50 mg of the catalyst. The tube was heated with an electric furnace at 2 °C min^{-1}, and the amount of H_2 consumed was monitored with a TC detector of a Shimadzu 4CPT gas chromatograph. Leaching of ruthenium species from the catalysts during the reaction was investigated by the ICP atomic emission spectroscopic analysis by using a Shimadzu ICPS-1000III analyzer. The products of catalytic runs were analyzed by GC-MS (Shimadzu GC-MS Parvum 2, DB-1 capillary column, i.d. 0.33 mm, length 25 m, at 50–250 ^oC) and gas chromatography (GL Sciences GC353, Inertcap 17 capillary column, i.d. 0.25 mm, length 30 m at 50–250 ^oC).

1.4.3 Preparation of supported Ru catalysts

Supported catalysts were prepared by the impregnation method. 1.0 g of CeO_2, prepared by the treatment of cerium(III) nitrate with aqueous ammonia, was added to a solution of 42 mg of $Ru_3(CO)_{12}$ in 10 mL of THF in air at room temperature. After impregnation, the resulting light yellow powder was calcined in air at 400 ^oC for 30 min

to afford the Ru(2.0 wt%)/CeO_2 catalyst as a dark brown powder.

1.4.4 General procedure for catalytic transfer-allylation–isomerization reaction

Homoallyl alcohol **1** (1.0 mmol), aldehyde **2** (0.50 mmol), and mesitylene (2.0 mL) were placed in a glass Schlenk tube with a balloon under an argon atmosphere together with 125 mg of the Ru(2.0 wt%)/CeO_2 catalyst (0.025 mmol as Ru). The reaction mixture was stirred on a hot stirrer at 170 ^{o}C with a cooling block for 24 h. The products were identified by GC-MS and NMR measurements, and quantified by GC using naphthalene as an internal standard.

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Chapter 2

Recyclable solid ruthenium catalysts for the direct arylation of aromatic C–H bonds

2.1 Introduction

The development of new environmentally benign processes for synthesizing organic compounds is one of the most important issues currently facing synthetic chemists [1].

The formation of C–C bonds by the direct activation of less reactive hydrocarbon C–H bonds by using homogeneous transition-metal catalysts has also attracted considerable attention in modern synthetic chemistry [2]. On the other hand, if efficiencies comparable to those achieved with homogeneous catalysis can be realized, heterogeneous catalysis is quite attractive, because the catalysts can be readily separated from reaction media and re-used [3]. Several solid catalysts have been reported to be effective for use in conventional C–C bond-forming reactions [4]; the arylation of heteroarenes or phenols over heterogeneous Ni, Pd or Ru catalysts have been reported [5]. However, to the best of our knowledge, there have been no previous reports of C–C bond formation by using chelation-assisted activation of stable aromatic C–H bond by solid ruthenium catalysts. Chapter 1 described a heterogeneous Ru/CeO_2-catalyzed transfer-allylation of homoallyl alcohols into aldehydes [6], in which the active species was considered to be a low-valent Ru species generated in situ from a Ru(IV) oxide

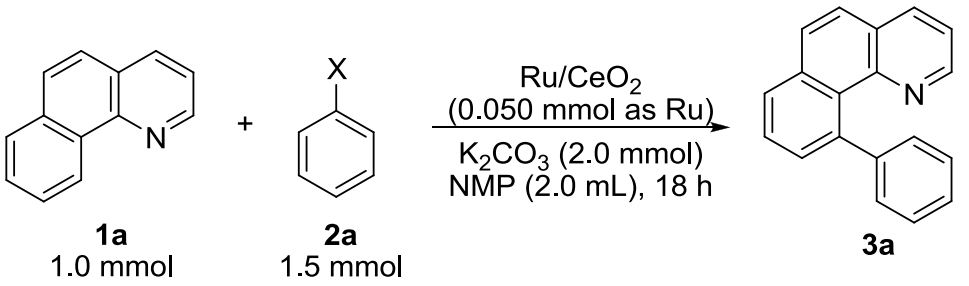
species on CeO_2.

In this chapter, the Ru/CeO_2-catalyzed the nitrogen-directed arylation of aromatic C–H bonds with aryl halides is described. This reaction, for which low-valent Ru complex catalysts are quite effective [7], is one of the most ecological and economical methods available for preparing unsymmetrical biaryls [7–9]. The results in this chapter imply that solid Ru/CeO_2 catalyst can be a good alternative to homogeneous Ru catalysts, which are known to be effective for a wide range of C–C bond-forming reactions.

2.2 Results and discussion

The reaction of benzo[*h*]quinoline (**1a**) with chlorobenzene (**2a**) in *N*-methyl-2-pyrrolidone (NMP) at 170 ^{o}C for 18 h in the presence of a Ru/CeO_2 catalyst prepared by using $Ru_3(CO)_{12}$ as a Ru precursor gave the arylated product **3a** selectively in a yield of 61% (Table 1, entry 1). The addition of a small amount of PPh_3 to the reaction mixture facilitated the reaction and gave **3a** quantitatively (entry 2). The reactions of **1a** with bromobenzene (**2a'**) or iodobenzene (**2a"**) also produced **3a** quantitatively (entries 3 and 4). The catalytic activity was greatly affected by the use of different Ru precursors. Catalysts prepared from Cl-containing Ru precursors such as $[RuCl_2(CO)_3]_2$, $[RuCl_2(p\text{-cymene})]_2$ or $RuCl_3{\cdot}nH_2O$ gave **3a** in higher yields than that prepared from Ru(cod)(cot) (entries 5–8). The reaction that was carried out at 150 ^{o}C gave only a trace amount of the biaryl product (entry 9); this indicates that a high reaction temperature is required to generate the highly active catalytic species in situ from the ruthenium(IV) species supported on CeO_2 [6,10].

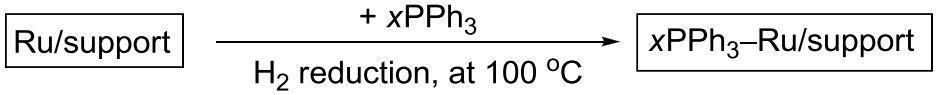
Table 1: Effect of ruthenium precursor.[a]



Entry	Ru precursor	PPh_3 (mmol)	**2**	X	Temp. (^oC)	Yield (%)[b]
1	$Ru_3(CO)_{12}$	-	**2a**	Cl	170	61
2	$Ru_3(CO)_{12}$	0.10	**2a**	Cl	170	99
3	$Ru_3(CO)_{12}$	0.10	**2a'**	Br	170	99
4	$Ru_3(CO)_{12}$	0.10	**2a"**	I	130	99
5	$RuCl_3 \cdot nH_2O$	-	**2a**	Cl	170	89
6	$[RuCl_2(CO)_3]_2$	-	**2a**	Cl	170	84
7	$[RuCl_2(p\text{-cymene})]_2$	-	**2a**	Cl	170	69
8	Ru(cod)(cot)	-	**2a**	Cl	170	25
9	$Ru_3(CO)_{12}$	-	**2a**	Cl	150	trace

[a] CeO_2 was prepared by using an aqueous solution of NH_3.[b] Determined by GLC and based on **1a**.

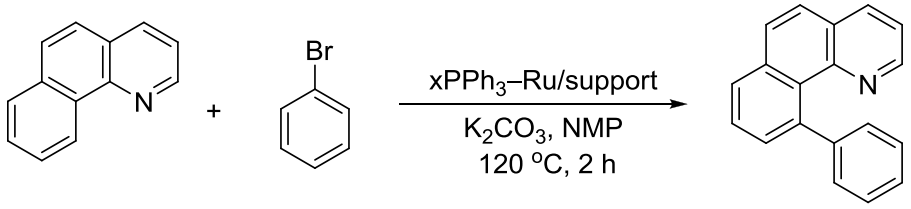
Next, the effects of pretreatment of the Ru/CeO_2 catalyst were examined, and the PPh_3 modification of Ru/CeO_2 was found to greatly increase the catalytic activity. PPh_3-modified solid Ru catalysts were prepared as follows: Treatment of Ru/support at 100 °C for 20 min in the presence of PPh_3 in a hydrogen atmosphere afforded PPh_3-modified Ru catalysts, designated as *x*PPh_3–Ru/support (*x* = molar ratio of PPh_3:Ru; Scheme 1).



Scheme 1 . Preparation of PPh_3–Ru/support catalysts.

In the presence of the PPh_3-modified Ru/CeO_2 catalyst, $3PPh_3$–Ru/CeO_2, the reaction of **1a** with **2a'** gave **3a** in a yield of 81% under much milder conditions: 120 °C for 2 h (Table 2, entry 1). The PPh_3-modified solid Ru catalyst supported on ZrO_2 gave **3a** in a good yield (entry 2), but catalysts supported on SiO_2, Al_2O_3, TiO_2 or MgO (entries 3–6) did not show any catalytic activity [11]. The precipitant used for the preparation of CeO_2 also affected the catalytic activity, with KOH gaving the best results (entry 9). Furthermore, the molar ratio of PPh_3 used for the modification, as well as the pretreatment conditions, significantly affected the catalytic activity; $3PPh_3$–Ru/CeO_2 showed the highest activity (entries 9–11). Note that it has also been reported that C–H alkylation catalyzed homogeneous ruthenium complexes by is also affected by the number of phosphine ligands coordinated to the Ru center [12]. Catalysts reduced in the absence of PPh_3 did not produce **3a** at all (entry 12), even if PPh_3 was added to the reaction mixture (entry 13). Note that the quantity of Ru species that leached into the solution after the reaction shown in entry 9 was 0.00065 mmol (2.6% of Ru species in the fresh catalyst), as calculated by ICP-AES analysis.

Table 2. Direct arylation by PPh_3-modified solid Ru catalysts.[a]



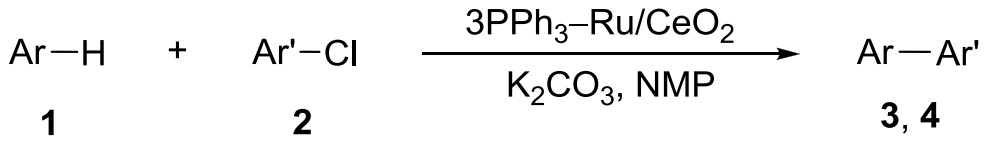
1a **2a'** **3a**

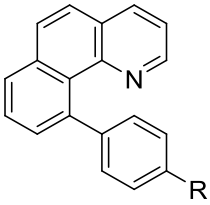
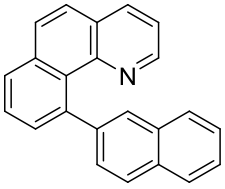
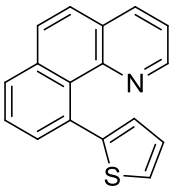
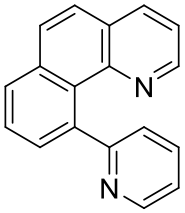
Entry	*x*	Ru precursor	Support[b]	Yield (%)[c]
1	3	$Ru_3(CO)_{12}$	CeO_2 (NH_3)	81
2	3	$Ru_3(CO)_{12}$	ZrO_2 (JRC-ZRO-3)	60
3	3	$Ru_3(CO)_{12}$	SiO_2 (Cabosil)	0
4	3	$Ru_3(CO)_{12}$	TiO_2 (JRC-TIO-4)	0
5	3	$Ru_3(CO)_{12}$	Al_2O_3 (JRC-ALO-8)	0
6	3	$Ru_3(CO)_{12}$	MgO (NH_3)	0
7	3	$[RuCl_2(CO)_3]_2$	CeO_2 (NH_3)	68
8	3	$Ru_3(CO)_{12}$	CeO_2 (KOH)	76
9	3	$[RuCl_2(CO)_3]_2$	CeO_2 (KOH)	98 (99)[d]
10	2	$[RuCl_2(CO)_3]_2$	CeO_2 (KOH)	39
11	4	$[RuCl_2(CO)_3]_2$	CeO_2 (KOH)	63
12	0	$[RuCl_2(CO)_3]_2$	CeO_2 (KOH)	0
13[e]	0	$[RuCl_2(CO)_3]_2$	CeO_2 (KOH)	0

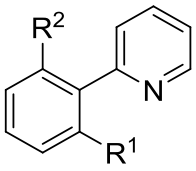
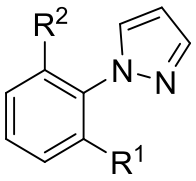
[a] *Reaction conditions:* **1a** (0.50 mmol), **2a'** (0.75 mmol), *x*PPh_3–Ru/support (0.025 mmol as Ru atom), K_2CO_3 (1.0 mmol), NMP, 2.0 mL. [b] The support or precipitant used to prepare the support is shown parenthesis. [c] Determined by GLC and based on **1a**. [d] *Reaction condition*: **1a** (1.0 mmol), **2a'** (1.5 mmol), *x*PPh_3–Ru/CeO_2 (0.050 mmol as Ru atom), K_2CO_3 (2.0 mmol), NMP (2.0 mL). [e] 0.075 mmol of PPh_3 was added to the reaction mixture.

The catalytic reactions of chloroarenes were examined by using the $3PPh_3$–Ru/CeO_2 catalyst, which showed the highest activity in Table 2 (entry 9), and the results are summarized in Table 3. While the reaction with chlorobenzene at 120 ^oC provided arylated product **3a** in a moderate yield (entry 1), the reaction at 140 ^oC proceeded efficiently to afford **3a** in 94% yield within 6 h (entry 2). Various chloroarenes with *para* functional groups and 2-chloronaphthalene could also be used in this reaction and the desired products **3b**–**3g** were obtained in excellent yields (entries 3–8). Also, the reactions with heterocyclic chlorides, 2-chlorothiophene and 2-chloropyridine, gave **3h** and **3i**, respectively, with satisfactory yields (entries 9 and 10). The reactions with other directed C–H activation substrates were also examined; treatment of 2-phenylpyridine (**1b**) and 1-phenyl-2-pyrazol (**1c**) with 4-chloroacetophenone (**2d**) produced mixtures of the mono- (**3j** and **3k**) and diarylated (**4j** and **4k**) products (entries 11 and 12).

Table 3. Direct arylation with aryl chlorides.[a]



Entry	Product		Time (h)	Yield (%)[b]
1[c]		**3a** (R = H)	12	58[d]
2		**3a** (R = H)	6	94[d]
3		**3b** (R = Me)	6	96
4		**3c** (R = OMe)	12	96
5		**3d** (R = COMe)	3	95
6		**3e** (R = CO_2Me)	5	91
7		**3f** (R = CF_3)	12	86
8		**3g**	5	98
9		**3h**	4	98
10		**3i**	6	53

11		**3j** (R^1 = H, R^2 = 4-$MeCOC_6H_4$) **4j** (R^1, R^2 = 4-$MeCOC_6H_4$)	3	94 (74 : 26) [e]
12		**3k** (R^1 = H, R^2 = 4-$MeCOC_6H_4$) **4k** (R^1, R^2 = 4-$MeCOC_6H_4$)	5	84 (60 : 40) [e]

[a] Reaction condition: **1**, 0.50 mmol; **2**, 0.75 mmol; 3PPh_3–Ru/CeO_2, (0.025 mmol as Ru atom); K_2CO_3, 1.0 mmol; NMP, 2.0 mL; 140 ^oC. [b] Isolated yield based on **1**. [c] Reaction at 120 ^oC. [d] Yield determined by GLC. [e] Molar ratio of **3** : **4**.

It is important to investigate whether or not the reaction actually occurs on the solid surface. To this end, hot filtration of the solid catalyst was carried out (Figure 1): After the reaction of **1a** and **2a'** in the presence of $3PPh_3$–Ru/CeO_2 at 120 ^oC had proceeded for 0.5 h, hot filtration completely suppressed further progress of the reaction. This result strongly suggests that the catalyst works heterogeneously.

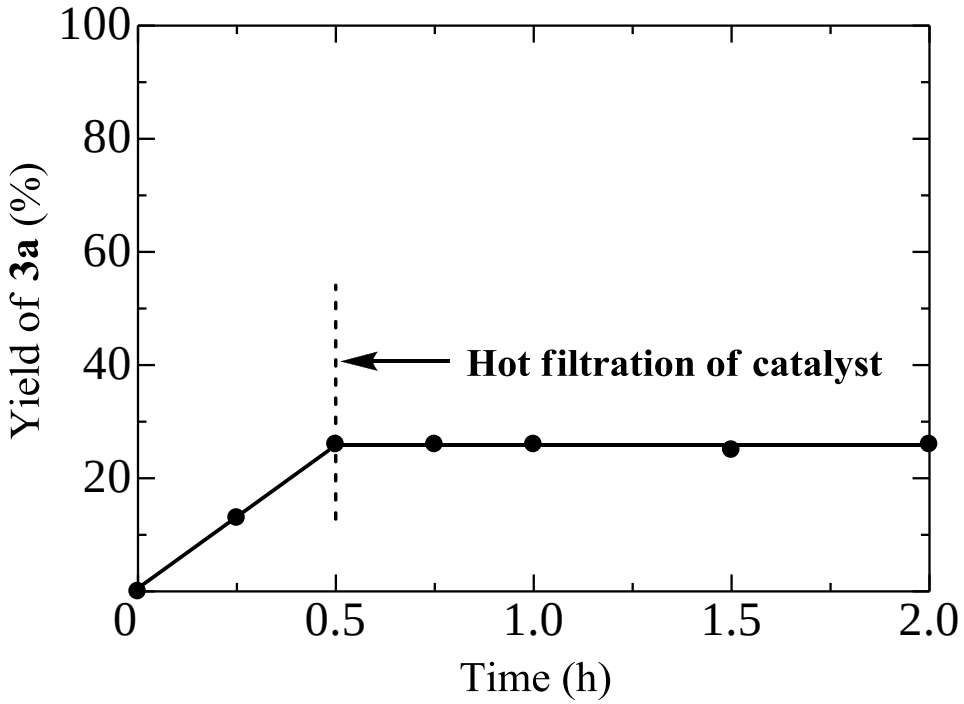
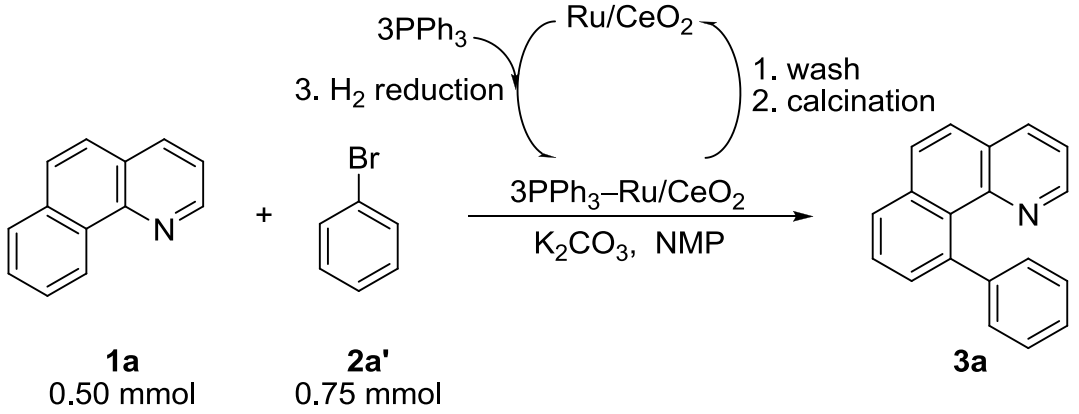


Figure 1. Result of the hot filtration test of Ru/CeO_2 catalyst.

One of the major advantages of solid catalysts is their recyclability. After performing the reaction under the condition shown in Table 2, entry 9, the solid catalyst was separated from the reaction mixture by centrifugation and washed with diethyl ether and methanol/H_2O. The resulting solid was calcined in air at 400 ^oC for 30 min to recover Ru/CeO_2. Modification by PPh_3 was then performed through the aforementioned procedure to give the PPh_3–Ru/CeO_2 catalyst for reuse. As shown in Scheme 2, the catalyst was recyclable and produced the biaryl product quantitatively within short reaction periods. Furthermore, at a higher temperature of 170 ^oC, the reaction went to completion within 0.5 h and the catalyst could be used at least three times without any loss of activity.



Scheme 2 . Recycle of solid Ru catalyst for the direct arylation of aromatic C–H bonds.

The catalytic systems were analyzed by various spectroscopic methods. XRD patterns of supported-Ru catalysts prepared from $Ru_3(CO)_{12}$ are shown in Figure 2. Although the peaks due to crystalline RuO_2 were observed for the Ru catalysts supported on ZrO_2, SiO_2, Al_2O_3 and MgO, they did not appear for Ru/CeO_2. This indicates that Ru species on CeO_2 are highly dispersed. Although the peaks due to RuO_2 were not observed on Ru/TiO_2, this catalyst did not show any catalytic activity. Note that, the BET surface areas of the Ru/CeO_2, Ru/ZrO_2, Ru/SiO_2, Ru/Al_2O_3, Ru/TiO_2, and Ru/MgO catalysts were 92, 108, 259, 144, 46, and 42 m^2g^{-1}, respectively.

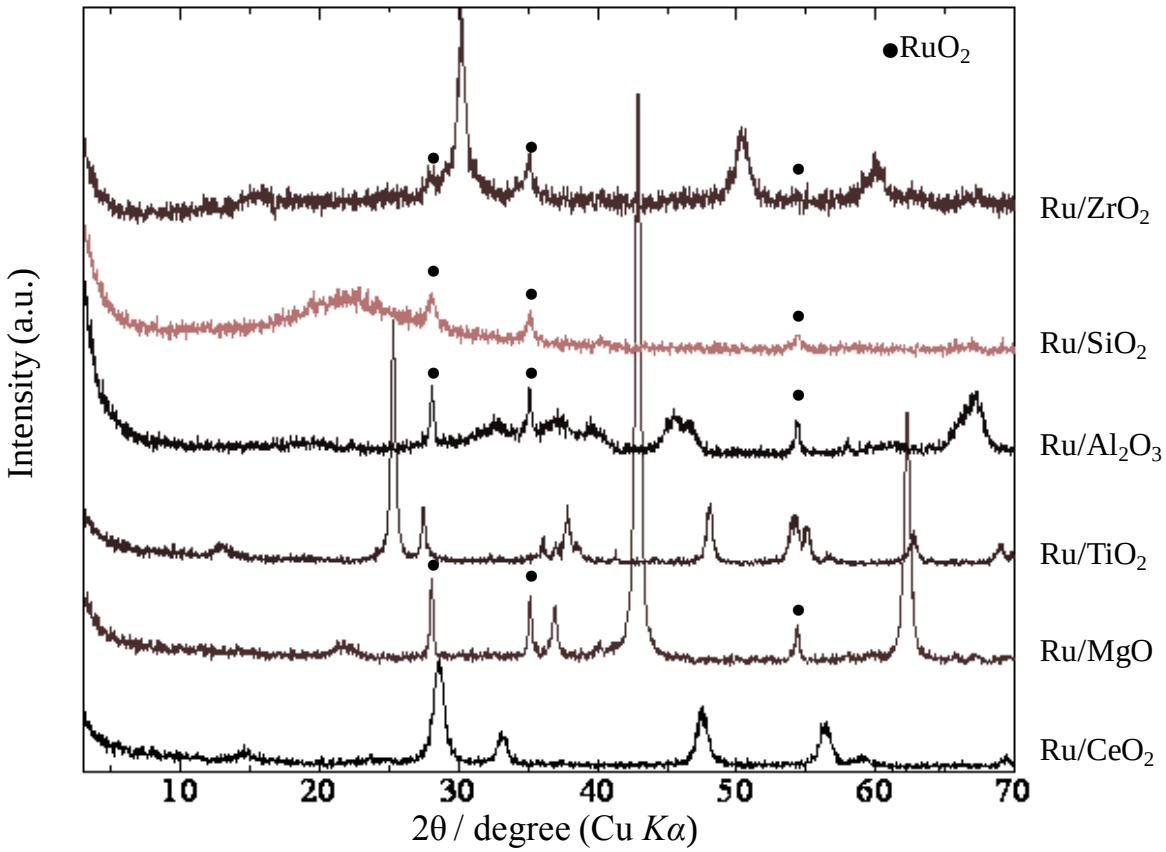


Figure 2. XRD patterns of Ru/supports.

The H_2-TPR profiles of the supported Ru catalysts prepared from $Ru_3(CO)_{12}$ are shown in Figure 3. For Ru/CeO_2 and Ru/ZrO_2 that showed catalytic activities for the title reaction, the reduction peaks appeared at <60 ^oC, whereas the other supported-Ru catalysts were reduced at >70 ^oC. This indicates that Ru species on CeO_2 or ZrO_2 are reduced much easily.

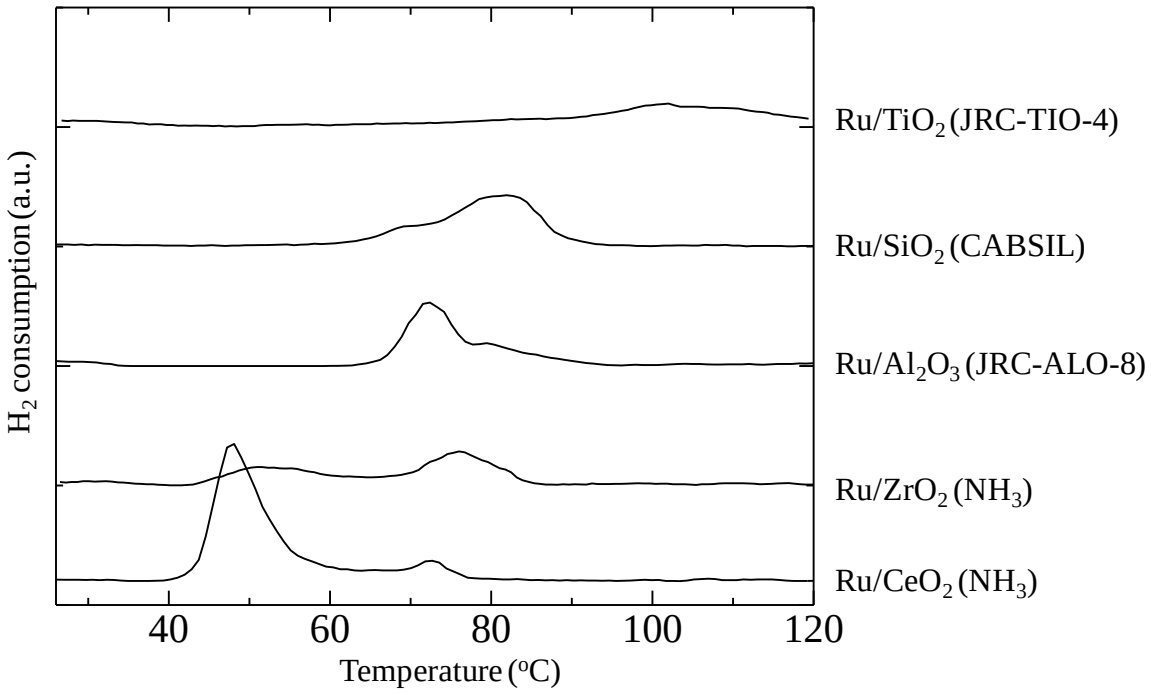


Figure 3. TPR profiles of supported Ru catalysts.

The H_2-TPR profiles of Ru/CeO_2 catalysts prepared from two different Ru precursors, $Ru_3(CO)_{12}$ and $[RuCl_2(CO)_3]_2$, are shown in Figure 4. For the both precursors, most of the ruthenium species on ceria was reduced at <100^oC, whereas bulk ruthenium(IV) oxide was reduced at 105 ^oC (data not shown).

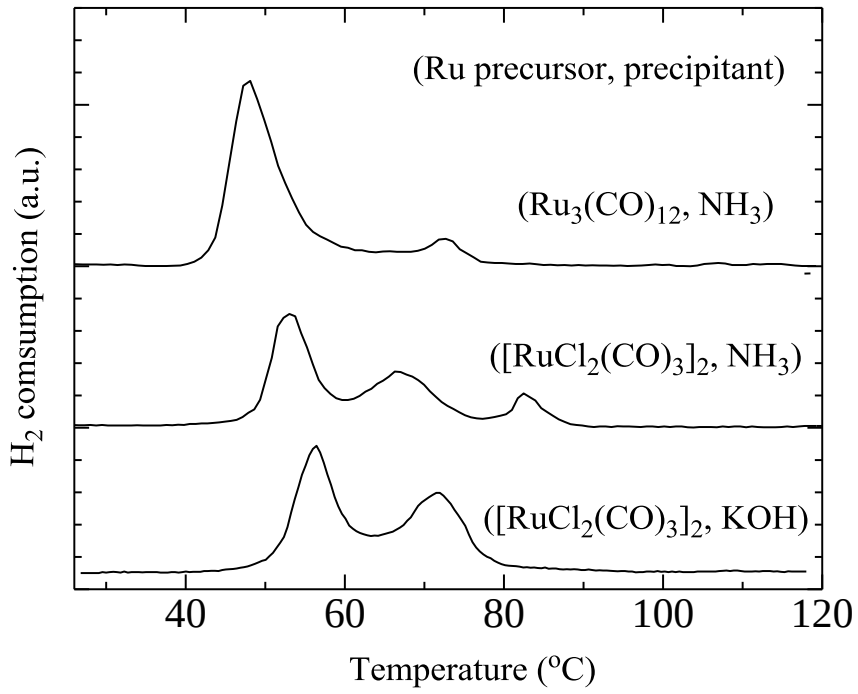


Figure 4. TPR profiles of Ru/CeO_2 prepared from different Ru precursors.

The Ru/CeO_2 catalysts prepared from $Ru_3(CO)_{12}$ and $[RuCl_2(CO)_3]_2$ were also characterized by nitrogen gas adsorption/desorption. The results are summarized in Table 4. All of the Ru/CeO_2 catalysts showed typical type IV nitrogen adsorption/desorption isotherms, indicating that their pore sizes distributed in the mesopore region.

Table 4. Characterization data by nitrogen gas adsorption/desorption of Ru/CeO_2 catalysts.

Entry	Ru precursor	Precipitant	Surface area (m^2g^{-1})	Pore volume (cm^3g^{-1})	Average pore radius (nm)
1	$Ru_3(CO)_{12}$	NH_3	79	0.137	3.5
2	$[RuCl_2(CO)_3]_2$	NH_3	69	0.147	4.4
3	$Ru_3(CO)_{12}$	KOH	91	0.162	2.4
4	$[RuCl_2(CO)_3]_2$	KOH	108	0.150	2.9

Diffuse reflectance FTIR spectra (900–1100 cm^{-1}) of Ru/CeO_2 (KOH) prepared from $[RuCl_2(CO)_3]_2$ before and after the reaction and recovered Ru/CeO_2 were shown in Figure 5. The distinct peak at 975 cm^{-1} attributed to Ru=O species was observed in fresh Ru/CeO_2. However, the peak disappeared in Ru/CeO_2 after the reaction. This result suggests that at the initial stage of the reaction, Ru species on CeO_2 was reduced to low-valent one, which showed the activity toward the reaction. In addition, the peak due to Ru=O species was also observed in the used Ru/CeO_2 after washing and calcination. Therefore, this catalyst was proved to be revived by washing and calcination.

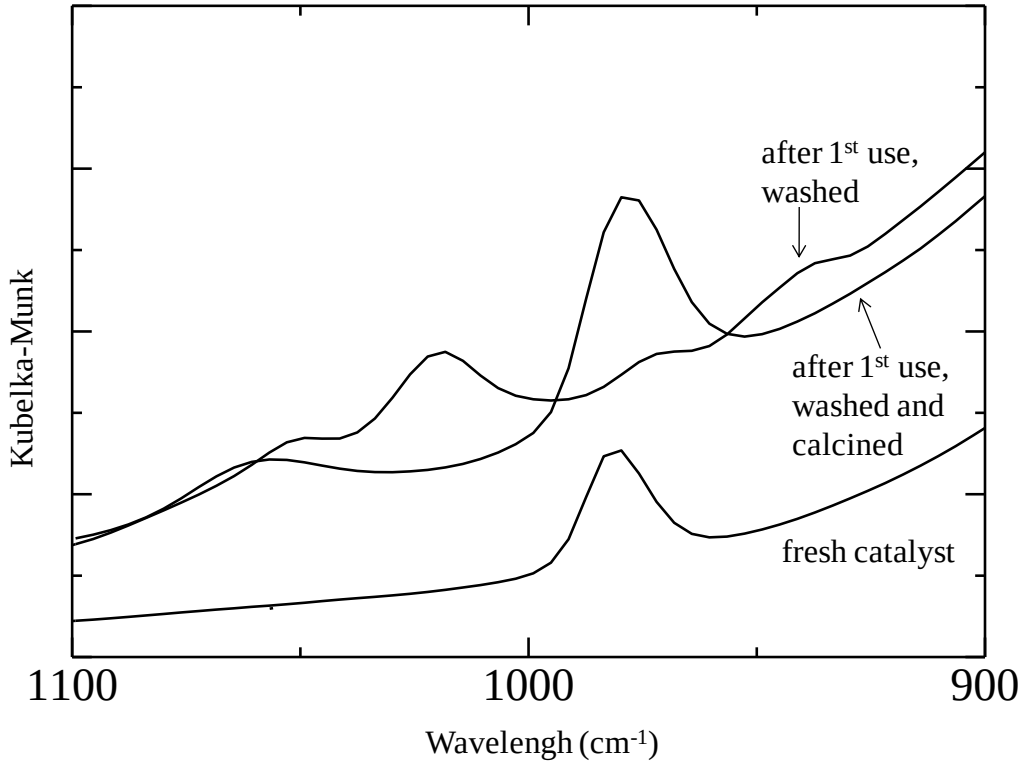


Figure 5. IR spectra of Ru/CeO_2.

The surface states of the Ru/CeO_2 (KOH) catalyst prepared from $[RuCl_2(CO)_3]_2$ before and after the reaction were investigated by XPS. Table 5 summarizes the surface composition and the binding energy of Ru species, whereas overlapping of C 1*s*, K 2*p*, and Ru 3*d* peaks partly disturbed the precise estimation of surface atomic ratios and binding energies. For the fresh catalyst, presence of Cl originating from the Ru precursor, $[RuCl_2(CO)_3]_2$, together with a small amount of K from KOH, a precipitant for ceria, was confirmed. The Ru $3d_{5/2}$ binding energy of 282.4 eV is consistent with the formation of Ru(IV) oxide on ceria [13]. The ratio of carbon atoms on the surface of the used catalyst before calcination was much higher than the fresh one indicating the strong deposition of carbonaceous materials on the surface. The Ru $3d_{5/2}$ peak appeared at 281.3 eV, indicating the formation of reduced species during the reaction, probably Ru(II) not Ru(0) [13]. Note that surface ratio of potassium atoms significantly increased, probably due to the deposition of K species from K_2CO_3, while surface chloride species were found to be removed by washing after the reaction. After calcination in air, a part of carbonaceous species was removed, and the Ru $3d_{5/2}$ peak appeared at 282.5 eV, again. Note that there were no sign of residual phosphorous species on the surface of these catalysts, indicating that PPh_3 was completely removed from the surface by thorough washing.

Table 5. XPS analysis of the Ru/CeO_2 catalyst prepared from $[RuCl_2CO)_3]_2$. [a]

Remarks	Surface concentration (atomic %)							Ru $3d_{5/2}$ (eV)
	C	Ru	Cl	K	P	Ce	O	
Rresh Ru/CeO_2	15.32	1.34	3.73	1.05	0.00	23.83	54.73	282.4
After 1st use[b] and washed	20.76	0.80	0.29	4.37	0.00	19.07	54.71	281.3
After 1st use, [b] washed and calcined	13.42	1.50	0.61	3.15	0.00	22.33	58.99	282.5

[a] Measured at -100 °C.
[b] Reaction condition is shown in Table 2.

The FTIR and XPS spectra revealed that the surface state of the used catalyst after calcination was almost identical to that of the fresh Ru/CeO_2 catalyst. Triphenylphosphine is found to be removed completely during the washing procedure, suggesting that triphenylphosphine weakly coordinates to the surface Ru species. Currently, it is speculated that calcination of the used catalysts required to regenerate surface ruthenium-oxo species as well as for removal of surface carbonaceous species.

2.3 Conclusions

In this chapter, the chelation-assisted direct arylation of an aromatic C–H bond by solid Ru catalysts is described. PPh_3-modified Ru/CeO_2 showed excellent catalytic activity, and various aryl chlorides could be used in the reaction. These results indicate that catalytically active species generated from Ru(IV) oxide species on CeO_2 can be an attractive alternative to homogeneous Ru catalysts. Moreover, the present heterogeneous catalytic system is quite advantageous from both environmental and practical perspectives, since these catalysts can be easily recovered and repeatedly used.

2.4 Experimental

2.4.1 Materials and methods

All manipulations were performed under an argon atmosphere using standard Schlenk techniques. Tririutheniumdodecacarbonyl, dichlorotricarbonylruthenium(II) dimer, di-μ-chlorobis[(*p*-cymene)chlororuthenium(II)] (Strem), ruthenium trichloride hydrate (Tanaka Kikinzoku), all the aryl halides (TCI), benzo[*h*]quinoline (TCI), 2-phenylpyridine, 1-phenyl-2-pyrazole (Aldrich), cerium(III) nitrate hexahydrate, potassium hydroxide, *N*-methyl-2-pyrrolidone, tetrahydrofurane (Wako), potassium carbonate, aqueous ammonia solution (28%) (Nacalai) were obtained commercially and used without further purification. Ru(cod)(cot) was prepared as described in the literature [14]. Ceria was prepared by treating a solution of cerium(III) nitrate hexahydrate (12.6 g, 29 mmol) in 400 mL of deionized water with 38 mL of 28% aqueous ammonia with stirring for 1 h at room temperature. The resulting precipitates were collected by centrifugation and then air-dried overnight at 80 ^{o}C. The product was

heated in a box furnace at a rate of 10 ^{o}C min^{-1} and maintained at 400 ^{o}C for 30 min to afford ceria in an excellent ceramic yield. Magnesium oxide was prepared from magnesium nitrates by a method similar to that used to obtain ceria. Zirconia (JRC-ZRO-3), titania (JRC-TIO-4), γ-alumina (JRC-ALO-8) and silica (Cabosil) were used as received.

2.4.2 Characterizations

The products of catalytic runs were analyzed by GC-MS (Shimadzu QP 2010, CBP10-S25-050 capillary column, i.d. 0.33 mm, length 25 m, at 50–250 ^{o}C) and gas chromatography (GL Sciences GC353, Inertcap 17 capillary column, i.d. 0.25 mm, length 30 m at 50–250 ^{o}C). NMR spectra were recorded on a JEOL JNM-EX-400 (FT, 400 MHz (^{1}H), 100 MHz (^{13}C)) instrument. Chemical shifts (δ) are referenced to $SiMe_4$. High-resolution mass spectra (FAB) were recorded on a JEOL SX102A spectrometer with *m*-nitrobenzyl alcohol (*m*-NBA) as a matrix. FT-IR spectra were recorded using a Nicolet Magna-IR 560 FT-IR spectrometer.

The oxide catalysts were analyzed by XRD, nitrogen gas adsorption, H_2-TPR and FTIR. X-ray powder diffraction analyses were performed using Cu *K*α radiation and a carbon monochromator (XRD: XD-D1, Shimazu). Nitrogen adsorption/desorption isotherms were obtained with a computer-controlled automatic gas sorption system, Quantachrome NOVA 4200e. Samples were degassed at 300 ^{o}C for 2 h just before the measurements. Temperature-programmed reduction (TPR) was carried out with a flow-type reactor. Hydrogen (1.9 vol.% in Ar under atmospheric pressure at 30 mL min^{-1}) was passed through a reaction tube containing the catalyst. The tube was heated with an electric furnace at 2 °C min^{-1}, and the amount of H_2 consumed was monitored

with a TC detector on a Shimadzu 4CPT gas chromatograph. Diffuse reflectance IR spectra were recorded using a Nicolet Magna-IR 560 FT-IR spectrometer with DRIFT optical configuration. X-ray photoelectron spectra (XPS) of the catalysts were acquired using an ULVAC-PHI 5500MT system equipped with a hemispherical energy analyzer using Mg *K*α radiation (15 kV, 400 W). Samples were mounted on indium foil and then transferred to an XPS analyzer chamber. Binding energies were referenced to the C 1s level of residual graphitic carbon [13].

Leaching of ruthenium species from the catalysts during the reaction was investigated by the ICP atomic emission spectroscopic analysis by using a Shimadzu ICPS-1000III analyzer.

2.4.3 Preparation of catalysts

Supported catalysts were prepared by the impregnation method. 1.0 g of support was added to a solution of $Ru_3(CO)_{12}$ (42 mg, 0.067 mmol) in 10 mL of THF in air at room temperature. After impregnation, the resulting powder was calcined in air at 400 ^oC for 30 min to afford the Ru/Support catalyst. When $[RuCl_2(CO)_3]_2$ and Ru(cod)(cot) were used as precursors, THF was used as a solvent for impregnation, while methanol was used with $RuCl_3 \cdot nH_2O$ and $[RuCl_2(p\text{-cymene})]_2$.

2.4.4 Preparation of PPh_3-modified Ru/Support catalyst

Ru/support was stirred in the presence of PPh_3 at 100 ^oC in a hydrogen atmosphere (1 bar) on a hot stirrer with a cooling block for 20 min to give PPh_3–Ru/support.

2.4.5 General procedure for direct arylation of aromatic C–H bonds by Ru/CeO_2

Benzo[*h*]quinoline **1a** (89.5 mg, 0.50 mmol), 4-chloroacetophenone **2d** (116 mg, 0.75 mmol), K_2CO_3 (138 mg, 1.0 mmol) and NMP (2.0 mL) were placed in a glass Schlenk tube (20 mL) under an argon atmosphere together with the $3PPh_3$–Ru/CeO_2 catalyst (0.025 mmol as Ru). The reaction mixture was stirred at 140 ^oC for 3 h on a hot stirrer with a cooling block. After the reaction, the reaction solution was separated from the reaction mixture by centrifugation and concentrated under reduced pressure. The products were isolated by column chromatography (hexane : EtOAc = 3 : 1, v/v) to give the product **3d** as a white solid (141.7 mg, 95%).

2.4.6 Recovery of $3PPh_3$–Ru/CeO_2 catalyst

After the reaction (*Scheme 2*), the solid was separated from the reaction mixture by centrifugation and completely washed with 10 mL of diethyl ether, 10 mL of methanol/H_2O (1 : 1, v/v) and 10 mL of diethyl ether, in this order. The resulting solid was dried overnight at 80 ^oC and calcined in air at 400 ^oC for 30 min to recover Ru/CeO_2. Modification by PPh_3 was then performed through the aforementioned procedure to give the PPh_3–Ru/CeO_2 catalyst for reuse.

2.4.7 Hot filtration tests

A 20 mL Schlenk tube was charged with benzo[*h*]quinoline **1a** (79.5 mg, 0.50 mmol), bromobenzene **2a'** (0.75 mmol), K_2CO_3 (138 mg, 1.0 mmol), the $3PPh_3$-Ru/CeO_2 catalyst (125 mg, 0.025 mmol as Ru), and NMP (2.0 mL) together with an internal standard (*o*-terphenyl, *ca*. 50 mg) under an argon atmosphere. The mixture was filtered, after the reaction was allowed to proceed for 30 min at 120 ^oC, through a

0.45 μm syringe filter (Millipore Millex LH) into another preheated Schlenk tube. The filtrate was stirred at 120 ^{o}C together with K_2CO_3 (138 mg, 1.0 mmol). The conversion and yields of the product after filtration were followed by GC and GC-MS analyses.

2.4.8 Characterization of new compounds (3e, 3f, 3g and 3i)

Methyl 4-(benzo[*h*]quinolin-10-yl)benzoate (3e): White solid; m.p. 105–106 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.37 (dd, J = 3.9, 1.5 Hz, 1H), 8.07 (m, 3H), 7.94 (d, J = 8.3 Hz, 1H), 7.85 (d, J = 8.8 Hz, 1H), 7.71–7.63 (m, 2H), 7.49 (d, J = 7.3 Hz, 1H), 7.41 (d, J = 8.4 Hz, 2H), 7.31 (dd, J = 8.0, 4.4 Hz, 1H), 3.99 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 167.6, 151.6, 146.9, 146.4, 140.5, 135.2, 134.9, 131.0, 128.8, 128.7, 128.4, 128.2, 127.4, 127.2, 127.0 126.1, 121.2, 52.0 FT-IR (KBr, cm^{-1}) 1713. HRMS: Calculated for $C_{21}H_{16}NO_2$ (M+H): 314.1181; found: 314.1179.

10-(4-(Trifluoromethyl)phenyl)benzo[*h*]quinoline (3f): White solid; m.p. 70–71 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.38 (dd, J = 3.9, 1.5 Hz, 1H), 8.08 (dd, J = 8.2, 1.9 Hz, 1H), 7.95 (d, J = 7.8 Hz, 1H), 7.86 (d, J = 8.7 Hz, 1H), 7.71–7.62 (m, 4H), 7.48 (d, J = 7.3 Hz, 1H), 7.44 (d, J = 7.8 Hz, 2H), 7.31 (dd, J = 8.3, 3.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 150.2, 146.9, 146.4, 140.2, 135.3, 135.0, 131.1, 129.0, 128.8, 128.2, 127.9, 127.6, 127.2, 127.1, 126.1, 124.3, 124.2, 123.4, 121.3 HRMS: Calculated for $C_{20}H_{13}NF_3$ (M+H): 324.1001; found: 324.1000.

10-(Naphthalen-2-yl)benzo[*h*]quinoline (3g): White solid; m.p. 118–119 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.31 (dd, J = 3.9, 1.5 Hz, 1H), 8.08 (dd, J = 8.2, 1.5

Hz, 1H), 7.96 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.92–7.86 (m, 4H), 7.76 (d, *J* = 8.8 Hz, 1H), 7.74–7.63 (m, 2H), 7.63 (dd, *J* = 7.3, 1.5 Hz, 1H), 7.50–7.46 (m, 2H), 7.43 (dd, *J* = 8.3, 1.5 Hz, 1H), 7.29 (dd, *J* = 7.8, 4.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 146.9, 146.7, 144.5, 141.4, 135.2, 135.0, 133.7, 132.1, 131.9, 129.4, 129.0, 128.3, 128.1, 128.0, 127.6, 127.2, 127.1, 126.0, 125.6, 125.5, 125.4, 125.1, 121.1 HRMS: Calculated for $C_{23}H_{16}N$ (M+H): 306.1283; found: 306.1288.

10-(Pyridin-2-yl)benzo[*h*]quinoline (3i): Light brown liquid. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.66 (dd, *J* = 4.4 Hz, 1H), 8.36 (dd, *J* = 4.4, 1.5 Hz, 1H), 8.07 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.97 (d, *J* = 7.8 Hz, 1H), 7.86 (d, *J* = 8.8 Hz, 1H), 7.71 (m, 3H), 7.63 (d, *J* = 5.8 Hz, 1H), 7.36 (d, *J* = 7.8 Hz, 1H), 7.30 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 164.1, 148.5, 147.0, 146.3, 140.3, 135.2, 134.8, 130.3, 129.1, 128.7, 128.1, 127.3, 127.1, 126.0, 123.9, 121.1, 120.9 HRMS: Calculated for $C_{18}H_{13}N_2$ (M+H): 257.1079; found: 257.1079.

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Chapter 3

Catalytic addition of aromatic C–H bonds to vinylsilanes in the presence of Ru/CeO_2

3.1 Introduction

Low-valent ruthenium species show unique catalytic properties and enable various organic transformations [1], such as C–C bond formations through cleavage of stable aromatic C–H bonds [2–4]. In particular, the $RuH_2(CO)(PPh_3)_3$-catalyzed selective addition of aromatic C–H bonds to unsaturated compounds has made it possible to rapidly construct carbon skeletons with excellent atom efficiency [3]. However, in preparing and handling such low-valent complexes, difficulties are often encountered because they are highly sensitive toward air and moisture. As an alternative approach, the *catalytically active* species, generated *in situ* from *catalytically inactive* but *air stable* Ru(II) complexes, has been adapted for these reactions [5], although it is essential to create an optimized coordination environment with suitable additives. However, problems remain in the separation of the catalysts from the products. In contrast, the use of solid catalysts, in particular simple solid oxides, are advantageous from environmental and industrial perspectives because they are thermally and chemically quite stable and can be readily separated from the products [6]. However, there have been few previous examples of reactions involving C–H bond activation in the presence of solid catalysts [7], and the development of new strategies for the preparation of *active*

low-valent Ru species on solid surfaces remains a challenge.

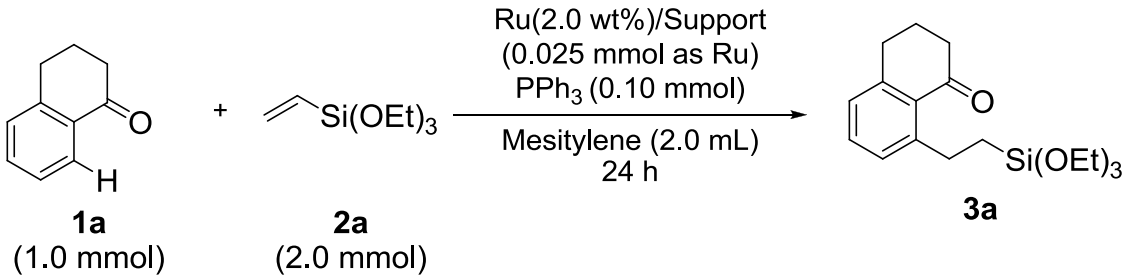
In the previous chapters, C–C bond-forming reactions through the activation of C–H or C–C bonds in the presence of simple metal oxide catalysts Ru/CeO_2 and Ru/ZrO_2 were described, whereas other solid Ru catalysts supported on SiO_2, Al_2O_3, MgO and TiO_2 showed no catalytic activities [8,9]. The catalytically active species in these reactions were considered to be low-valent Ru species generated from Ru(IV) species on CeO_2. From these backgrounds, various selective C–C bond forming reactions are expected to be realized on the solid catalysts, if the coordination sites of low-valent Ru species can be controlled by an appropriate choice of additives and pretreatment conditions. In this chapter, the catalytic addition of C–H bonds of aromatic ketones to vinylsilanes in the presence of Ru/CeO_2 is described. The reactions proceeded smoothly in association with appropriate phosphines to selectively give alkylated compounds in high yields. Furthermore, the pretreatment of Ru/CeO_2 under appropriate conditions increased the catalytic activities so markedly that the reaction rapidly went to completion at lower temperatures.

3.2 Results and discussion

The reaction of aromatic ketone (**1a**, 1.0 mmol) with vinylsilane (**2a** 2.0 mmol) in the presence of 125 mg of Ru(2.0 wt%)/CeO_2 (0.025 mmol as Ru) and 0.10 mmol of PPh_3 in mesitylene at 170 ^oC gave the product **3a** quantitatively (Table 1, entry 1). The product formed was regioselectively alkylated at the *ortho* position of the carbonyl group. The reaction below 160 ^oC resulted in a lower yield of **3a** (entries 2 and 3). Ru/ZrO_2 showed an activity comparable to that of the CeO_2-supported Ru catalyst (entry 4). On the other hand, Ru catalysts supported on SiO_2, Al_2O_3, TiO_2 and MgO

prepared by the same method as Ru/CeO_2 showed no catalytic activity (entries 5–8).

Table 1. Effect of supports.

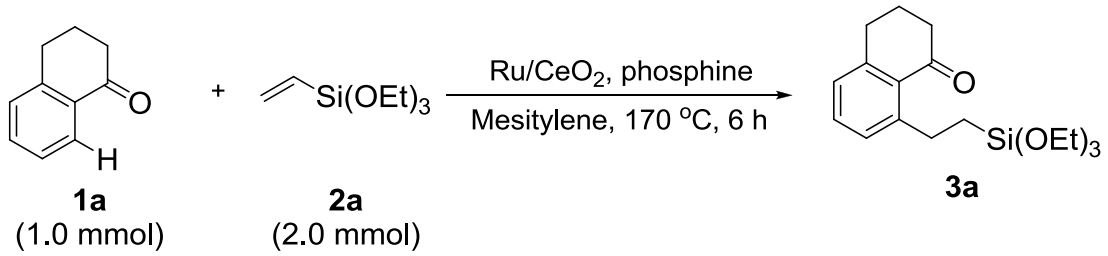


Entry	Support	Temperature (^oC)	Yield (%)[a]
1	CeO_2	170	99
2	CeO_2	160	50
3	CeO_2	150	46
4	ZrO_2	170	99
5	SiO_2	170	0
6	Al_2O_3	170	0
7	TiO_2	170	0
8	MgO	170	0

[a] Yield determined by GLC.

The class and amount of phosphorous additives greatly affected the reaction efficiency (Table 2). In the absence of PPh_3, the reaction did not take place at all (entry 1). When 0.10 mmol of PPh_3 (4.0 equivalents to Ru atom) was added, **3a** was obtained in the highest yield (entries 2–6). Besides PPh_3, P(*p*-F-C_6H_4)$_3$ was also suitable among the various phosphorous additives examined (entry 7). Other phosphorous additives, such as sterically hindered triarylphosphine (entry 9), alkyl phosphines (entries 10 and 11), diphosphine (entry 12), phosphite (entry 13), and phosphine oxide (entry 14), were not effective. Although the exact role of the phosphine is not clear at present, the results of phosphine screening for the catalytic reactions were very similar to those for homogeneous systems [3,5]. Thus, they are currently speculated to serve as ligands of catalytically active Ru species.

Table 2. Effect of phosphorous additives.[a]



1a (1.0 mmol) **2a** (2.0 mmol) **3a**

Entry	Additive	Additive loading (mmol)	Yield (%)[b]
1	None	-	0
2	PPh_3	0.025	28
3	PPh_3	0.050	47
4	PPh_3	0.075	60
5	PPh_3	0.10	78 (99)
6	PPh_3	0.15	67
7	P(*p*-F-C_6H_4)$_3$	0.10	66 (99)
8	P(*p*-tolyl)$_3$	0.10	7 (11)
9	P(*o*-tolyl)$_3$	0.10	0
10	P^{n}Bu$_3$	0.10	0
11	PCy_3	0.10	0
12	dppe[c]	0.050	0
13	$P(OPh)_3$	0.10	0
14	$O=PPh_3$	0.10	0

[a] *Reaction Conditions*: **1a** (1.0 mmol), **2a** (2.0 mmol), Ru/CeO_2 (0.025 mmol as Ru atom), mesitylene (2.0 mL), 170 °C, 6 h. [b] Determined by GLC (values in parenthesis refer to yields at time = 24 h).
[c] dppe = 1,2-bis(diphenylphosphino)ethane.

After the reaction for 24 h shown in entry 5 in Table 2, the amount of Ru species that leached into the solution, as estimated by ICP-AES, was 0.00075 mmol (3.0% of Ru species in the fresh catalyst). Hot filtration of the solid oxide after the reaction had proceeded for 3 h suppressed further progress of the reaction (Figure 1). This result indicates that the presence of solid Ru catalyst is indispensable for the reaction.

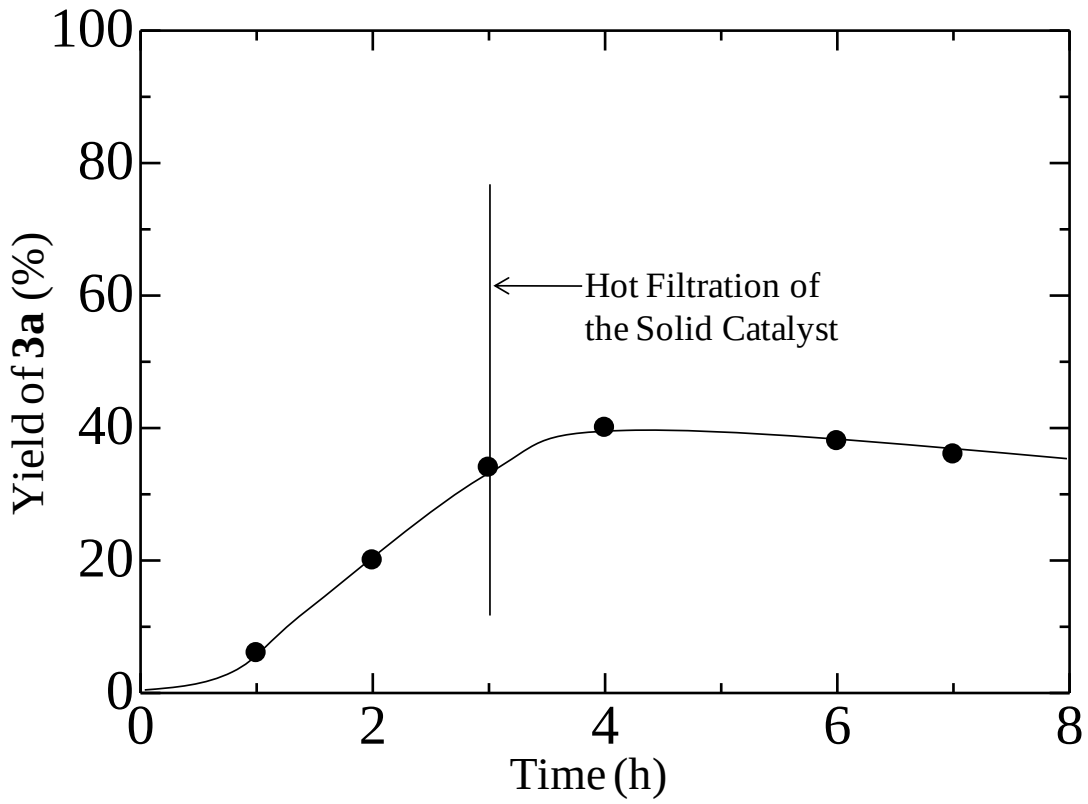
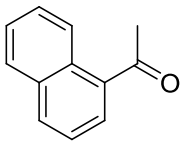
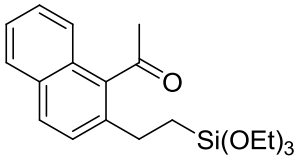
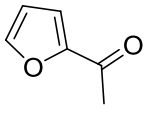
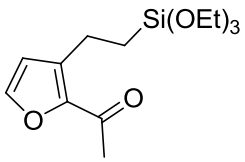
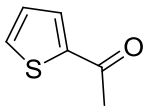
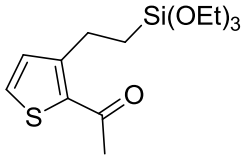
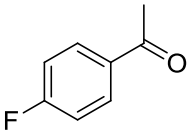
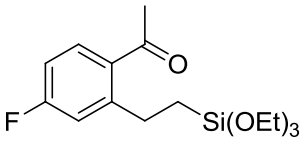
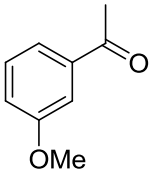
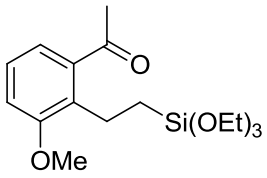
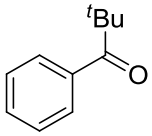
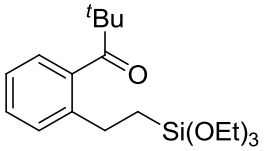
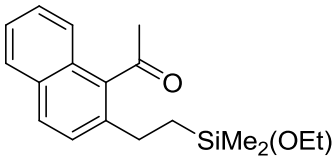


Figure 1. Hot filtration of Ru/CeO_2 catalyst.

The Ru/CeO_2-catalyzed reaction was applied to a range of aromatic ketones and vinylsilanes under the optimized conditions (Table 3). Both aromatic and heterocyclic ketones were found to react smoothly with triethoxyvinylsilane to afford the alkylated products in high yields (entries 1–3). For substrates **1e** and **1f** with two *ortho* C–H bonds, the corresponding products, **3e** and **3f,** were obtained with selectivities similar to those in the case of homogeneous systems (entries 4 and 5) [10]. From *tert*-butyl phenyl ketone **1g**, monoalkylated product was obtained selectively, probably because of steric hindrance [3b]. In addition, dimethylethoxyvinylsilane **2b** could also be used, and the reaction with **1b** afforded **3h** in high yield (entry 7). However, other alkenes, such as trimethylvinylsilane, allyltriethoxysilane and styrene, were not applicable under the present conditions.

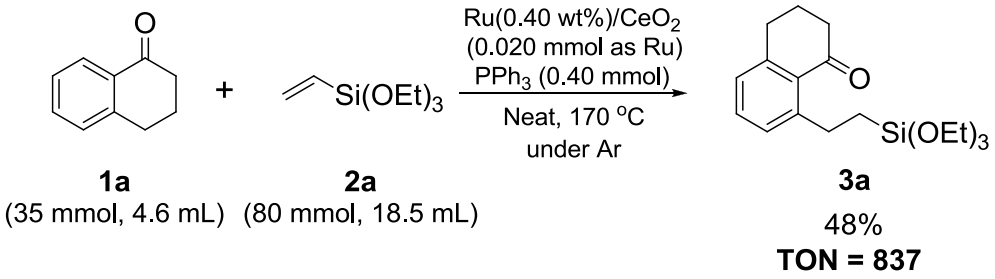
Table 3. Ru/CeO_2-catalyzed addition of C–H bonds of aromatic ketones to vinylsilanes.[a]

Entry	**1**	**2**	**3**	Yield (%)[b]
1	 **1b**	**2a**	 **3b**	96
2	 **1c**	**2a**	 **3c**	67

3	 **1d**	**2a**	 **3d**	94
4	 **1e**	**2a**	 **3e**	91 (53:47)[c]
5	 **1f**	**2a**	 **3f**	90 (100:0)[c]
6	 **1g**	**2a**	 **3g**	84 (100:0)[c]
7	**1b**	 **2b**	 **3h**	84

[a] *Reaction Conditions*: **1** (1.0 mmol), **2** (2.0 mmol), Ru/CeO_2 (0.025 mmol as Ru), mesitylene (2.0 mL), 170 ^oC, 24 h. [b] Isolated yields.
[c] The ratios of mono- to di-substituted products are given in parentheses.

From a practical point of view, it is very important that the reaction can be carried out on a large scale without solvent. The reaction of 35 mmol of **1a** with 80 mmol of **2a** proceeded efficiently and afforded **3a** with TON of 837 (Scheme 1).



Scheme 1. Large-scale reaction without solvent.

It is generally accepted that low-valent Ru species are responsible for the activation of an aromatic C–H bond [3,4]. The diffuse reflectance FTIR spectrum of Ru/CeO_2 before the reaction showed a distinct band at 975 cm^{-1}, which was assigned to Ru(IV)-oxo species [11]. The presence of such an oxo species was also proposed in Ru/ZrO_2 [12]. The peak disappeared after heating in mesitylene at 170 ^oC for 1.5 h, which suggests that the Ru(IV)-oxo species were reduced to low-valent species at the initial stage of the reaction. As described above, a high reaction temperature around 170 ^oC is needed to obtain alkylated compounds in high yields. This result indicates that high temperatures are essential for transforming Ru(IV)-oxo species on CeO_2 into catalytically active species.

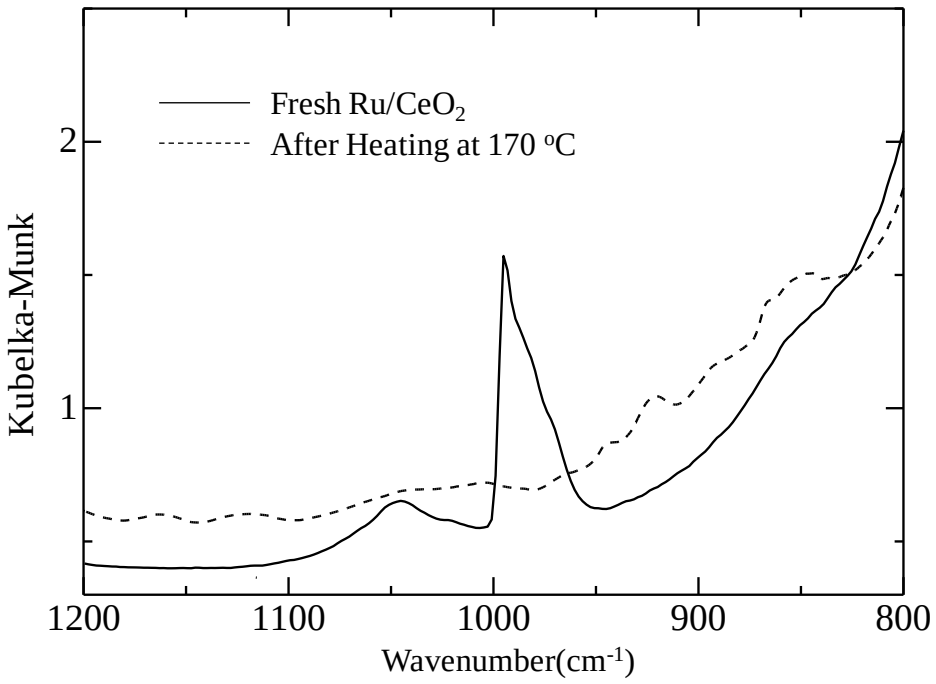
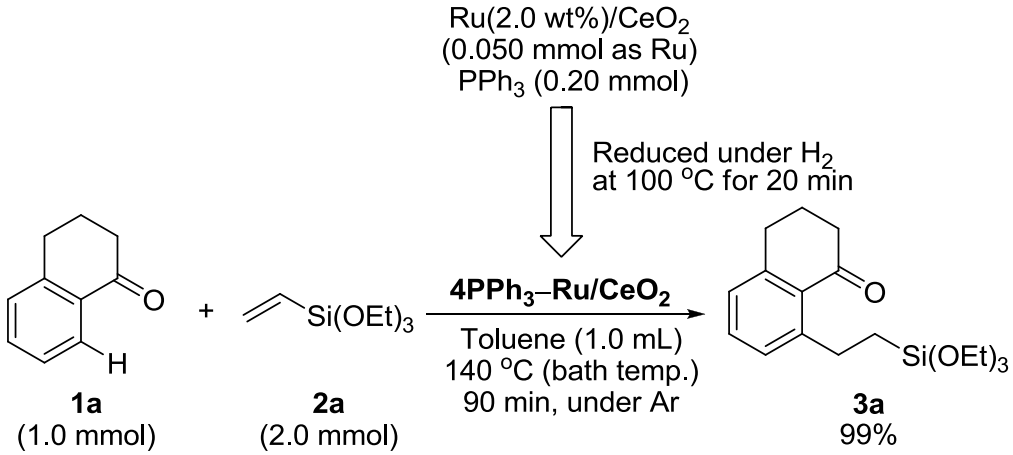


Figure 2. DRIFT spectra of Ru/CeO_2.

To generate highly active Ru species efficiently at lower temperature, the effects of pretreatment of Ru/CeO_2 were examined. The treatment of Ru/CeO_2 at 100 ^oC for 20 min under a hydrogen atmosphere in the presence of 4 equivalents of PPh_3 gave a PPh_3-modified catalyst (designated as $4PPh_3–Ru/CeO_2$). As in chapter 2 [9], the reaction of **1a** with **2a** was complete within 90 min, even at 140 ^oC (bath temperature) in the presence of $4PPh_3–Ru/CeO_2$ (Scheme 2). The amount of Ru species that had leached into the reaction mixture after the reaction was 2.0% of that from the fresh Ru/CeO_2. The catalytic activities were quite sensitive to the pretreatment conditions. For example, when Ru/CeO_2 reduced in the absence of PPh_3 was used for the reaction, the reaction did not occur at all, even in the presence of PPh_3.

$4PPh_3–Ru/ZrO_2$ showed comparable activity under identical conditions (yield of **3a**; 99% for 90 min). PPh_3-modified Ru catalysts supported on the other oxides listed in Table 1 did not show any activities.



Scheme 2. Effect of pretreatment of the Ru/CeO_2 catalyst.

After the reaction (entry 1 of Table 1), the Ru/CeO_2 catalyst was recovered from the reaction mixture by centrifugation and washed three times with 10 mL of diethyl ether, followed by drying overnight at 80 ^oC. The recovered catalyst was then calicined in air at 400 ^oC for 30 min to give a re-calcined catalyst. The reaction under conditions identical to those in entry 1 in Table 1 in the presence of the recovered Ru/CeO_2 catalysts gave **3a** in a very low yield (8%). The re-calcined Ru/CeO_2 catalyst did not show any catalytic activity. DRIFT spectra of the recovered Ru/CeO_2 catalysts with or without calcination are shown in Figure 3. The spectrum of the recovered and washed catalyst showed strong absorption bands at 800–1200 cm^{-1}, which could be assigned to Si–O stretching of siliceous materials such as silica or silsesquioxanes. The bands still existed after calcination, while the other bands at 1300–1700 cm^{-1} which are assigned to carbonate species disappeared.

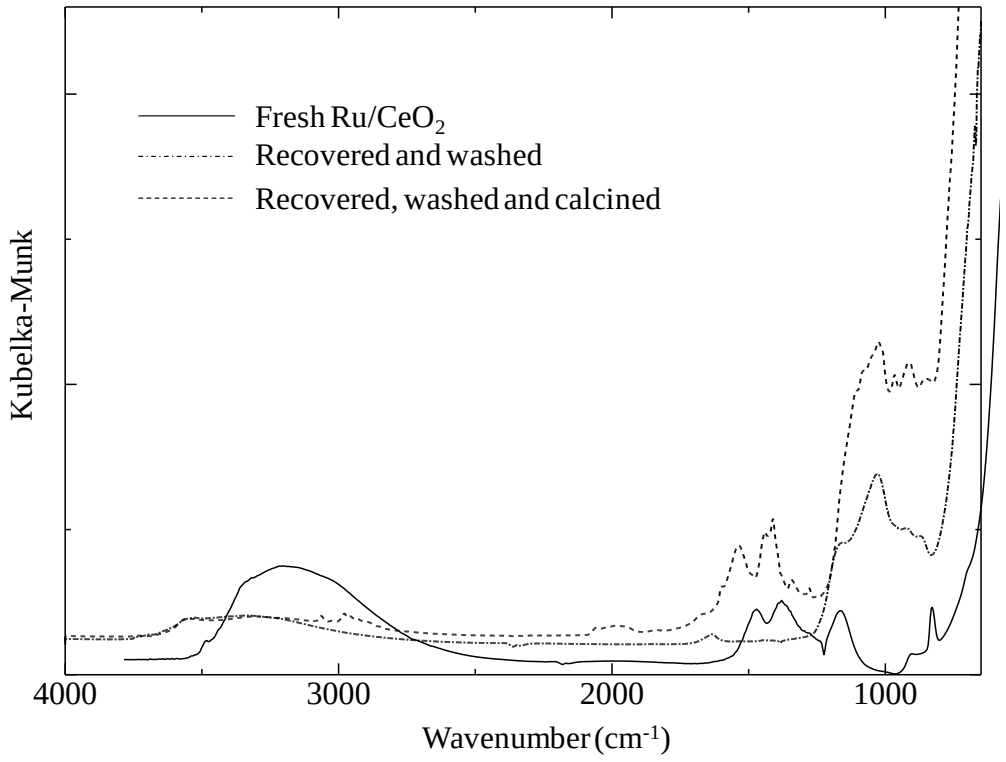


Figure 3. DRIFT-IR spectra of Ru/CeO_2 before and after the reaction.

Table 4 shows the result of XPS measurements. The atomic ratio of surface Ru species greatly decreased after the reaction. A significant amount of siliceous material was deposited on the surface of the recovered catalysts. There were no signs of residual phosphorous species on the recovered catalysts. Note that precise estimation of Ru $3d_{5/2}$ binding energies was hampered by the severe overlapping of C 1*s* peaks.

Table 4. Surface composition of the recovered Ru(2.0wt%)/CeO_2 catalysts estimated by XPS.

Remarks	Surface concentration (atomic %)					
	C	Ru	Si	P	O	Ce
Fresh Ru/CeO_2	16.54	1.33	0.00	0.00	54.56	27.56
Recovered and washed	20.84	0.66	4.22	0.00	55.70	18.58
Recovered, washed and calcined	9.87	0.59	6.93	0.00	64.48	18.12

The combined XPS and DRIFT results indicate that the surface Ru species in the recovered catalysts were irreversibly covered with siliceous materials derived from triethoxyvinylsilane. These results are in a sharp contrast to the cases in chapters 1 and 2, where Ru(IV)-oxo species were regenerated by calcination after the reaction to exhibit high catalytic activity. In the present case, the irreversible deposition of siliceous residues derived from vinylsilanes would prevent the regeneration of the Ru(IV)-oxo species.

3.3 Conclusion

As described in this chapter, the catalytic addition of a C–H bond of aromatic ketones to vinylsilanes can be achieved in the presence of Ru/CeO_2. The PPh_3-modified Ru/CeO_2 catalyst showed excellent catalytic activity without any significant leaching into the reaction mixture. The present results demonstrate the possible application of Ru/CeO_2 as a precursor of low-valent Ru species effective for various organic transformations.

3.4 Experimental

3.4.1 Materials and methods

All manipulations were performed under an argon atmosphere using standard Schlenk techniques. Triruthenium dodecacarbonyl (Strem), all of the aromatic ketones and vinylsilanes (TCI), cerium(III) nitrate hexahydrate, tetrahydrofuran (THF; Wako), and aqueous ammonia solution (28%) (Nacalai) were obtained commercially and used without further purification. Ceria was prepared by treating a solution of cerium(III) nitrate hexahydrate (12.6 g, 29 mmol) in 400 mL of deionized water with 38 mL of 28% aqueous ammonia with stirring for 1 h at room temperature. The resulting precipitates were collected by centrifugation and then dried overnight at 80 ^{o}C. The product was heated in a box furnace at a rate of 10 ^{o}C min^{-1} and maintained at 400 ^{o}C for 30 min to afford ceria in an excellent ceramic yield. Zirconium oxide and magnesium oxide were prepared from zirconium(IV) dinitrate oxide and magnesium nitrate by a method similar to that used to obtain ceria. Titania (JRC-TIO-4), γ-alumina (JRC-ALO-8) and silica (Cabosil) were used as received.

3.4.2 Physical and analytical measurements

The products of catalytic runs were analyzed by GC-MS (Shimadzu QP 2010, CBP10-S25-050 capillary column, i.d. 0.33 mm, length 25 m, at 50–250 ^{o}C) and gas chromatography (GL Sciences GC353, Inertcap 17 capillary column, i.d. 0.25 mm, length 30 m at 50–250 ^{o}C). NMR spectra were recorded on a JEOL JNM-EX-400 (FT, 400 MHz (^{1}H), 100 MHz (^{13}C)) instrument. Chemical shifts (δ) are referenced to $SiMe_4$.

Diffuse reflectance IR spectra were recorded using a Nicolet Magna-IR 560 FT-IR spectrometer with DRIFT optical configuration. X-ray photoelectron spectra (XPS) of the catalysts were acquired using an ULVAC-PHI 5500MT system equipped with a hemispherical energy analyzer using Mg *K*α radiation (15 kV, 400 W). Samples were mounted on indium foil and then transferred to an XPS analyzer chamber. Binding energies were referenced to the C 1s level of residual graphitic carbon [13].

Leaching of ruthenium species from the catalysts during the reaction was investigated by ICP atomic emission spectroscopic analysis by using a Shimadzu ICPS-1000III analyzer.

3.4.3 A typical method for the preparation of Ru/Support catalysts

Supported catalysts were prepared by an impregnation method. 1.0 g of support was added to a solution of $Ru_3(CO)_{12}$ (42 mg, 0.067 mmol) in 10 mL of THF in air at room temperature. After impregnation, the resulting powder was calcined in air at 400 ^{o}C for 30 min to afford the Ru(2.0 wt%)/Support catalyst.

3.4.4 Preparation of PPh_3-modified Ru/Support catalyst

Ru/Support was stirred in the presence of PPh_3 (*x* equivalent to Ru species) at

100 ^{o}C in a H_2 atmosphere (1 bar) on a hot stirrer with a cooling block for 20 min to give *x*PPh_3–Ru/Support.

3.5.5 Representative procedure for the addition of aromatic C–H bond to vinylsilane in the presence of Ru/CeO_2 catalysts

α-Tetralone **1a** (146 mg, 1.0 mmol), triethoxyvinylsilane **2a** (380 mg, 2.0 mmol), PPh_3 (26.2 mg, 0.10 mmol) and mesitylene (2.0 mL) were placed in a glass Schlenk tube (20 mL) under an argon atmosphere together with 125 mg of the Ru/CeO_2 catalyst (0.025 mmol as Ru). The reaction mixture was stirred at 170 ^{o}C for 24 h on a hot stirrer with a cooling block. The product was identified by GC-MS and NMR measurements, and quantified by GC using naphthalene as an internal standard

3.4.5 Hot filtration tests

A 20 mL Schlenk tube was charged with *α*-tetralone **1a** (146 mg, 1.0 mmol), triethoxyvinylsilane **2a** (380 mg, 2.0 mmol), the Ru/CeO_2 catalyst (125 mg, 0.025 mmol as Ru), PPh_3 (26.3 mg, 0.10 mmol) and mesitylene (2.0 mL) together with an internal standard (naphthalene, *ca*. 30 mg) under an argon atmosphere. After the reaction was allowed to proceed for 3 h at 170 ^{o}C, the mixture was filtered through a 0.45 μm syringe filter (Millipore Millex LH) into another preheated Schlenk tube. The filtrate was stirred at 170 ^{o}C. The conversion and yields of the product after filtration were followed by GC and GC-MS analyses.

3.4.6 Characterization of new compound (3h)

1-(2-(2-(ethoxydimethylsilyl)ethyl)naphthalen-1-yl)ethanone (**3h**): dark brown oil; ^{1}H

NMR (400 MHz, $CDCl_3$, ppm) δ 7.79–7.84 (m, 2H), 7.54 (d, J = 7.8 Hz, 1H), 7.4–7.5 (m, 2H), 7.37 (d, J = 8.2 Hz, 1H), 3.70 (q, J = 6.8 Hz, 2H), 2.68–2.72 (m, 2H), 2.64 (s, 3H), 1.02–1.24 (t, J = 6.8 Hz, 3H), 1.00–1.02 (m, 2H), 0.16 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 210.3, 139.9, 139.5, 133.9, 131.2, 131.0, 130.4, 129.2, 129.0, 127.6, 126.2, 60.5, 35.5, 29.1, 21.4, 20.7, 2.2 HRMS: Calculated for $C_{16}H_{19}OSi$ (M-OEt): 255.1205; found: 255.1208.

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Chapter 4

Transformation of Ru(IV)=O species supported on CeO_2 to active ruthenium catalysts for the addition of aromatic C–H bonds to unsaturated compounds

4.1 Introduction

From the perspective of sustainable chemistry, the development of greener and environmentally-benign catalytic processes for the synthesis of organic molecules has attracted considerable attention in the 21st century [1]. The use of supported metal catalysts is a promising strategy for decreasing the environmental load because of their simple preparation, high stability and facile recyclability, as well as minimal contamination of the products by metallic species [2]. However, since the electronic and steric control of active metal species on the surface of the solid support is much more difficult than with homogeneous complex catalysts, highly selective organic transformation with supported catalysts is still a challenge. Against this background, in the previous chapters, the properties of Ru/CeO_2 catalysts toward organic syntheses and the fine structure of Ru species on CeO_2 have been investigated [3a–c]. The specific feature of Ru/CeO_2 is the formation of Ru(IV)-oxo species on the surface of CeO_2, and the Ru(IV)-oxo species could be transformed into low-valent Ru species, which showed high activities for various types of organic transformations [3]. In contrast, other Ru

catalysts supported on SiO_2, Al_2O_3, TiO_2 or MgO did not show any activities for the reactions due to the absence of Ru(IV)-oxo species on the metal oxides [3]. These results indicate that different types of active Ru species could be generated from Ru(IV)-oxo species on CeO_2 through the appropriate choice of additives or pretreatment conditions.

Transition metal-catalyzed C–C bond-forming reactions that involve the cleavage and subsequent transformation of less-reactive C–H bonds are central issues in current synthetic chemistry [4]. In particular, the direct addition of aromatic C–H bonds to unsaturated carbon–carbon bonds (hydroarylation) is one of the most straightforward and atom-efficient methods for the synthesis of alkylated or alkenylated aromatic compounds [5]. Since the pioneering works with homogeneous Ru complexes, such as $RuH_2(CO)(PPh_3)_3$, by Murai, Kakiuchi, et al. [6], various catalytic systems that use transition-metal species and are effective for the hydroarylation of unsaturated compounds have been developed [7]. As described in chapters 2 and 3, Ru/CeO_2 that have been pretreated under a hydrogen atmosphere in the presence of PPh_3 (PPh_3-modified Ru/CeO_2) showed excellent catalytic activities for the addition of aromatic C–H bonds to alkoxyvinylsilanes as well as the direct arylation of aromatic C–H bonds with aryl chlorides [3b,c]. However, in our previous catalytic system for hydroarylation, recycling of the catalysts, which is a major advantage of solid catalysts, could not be achieved because of the irreversible deposition of siliceous residues derived from vinylsilanes on surface Ru species. Moreover, the catalytic system could not be applied to the reaction of unsaturated compounds other than alkoxyvinylsilanes.

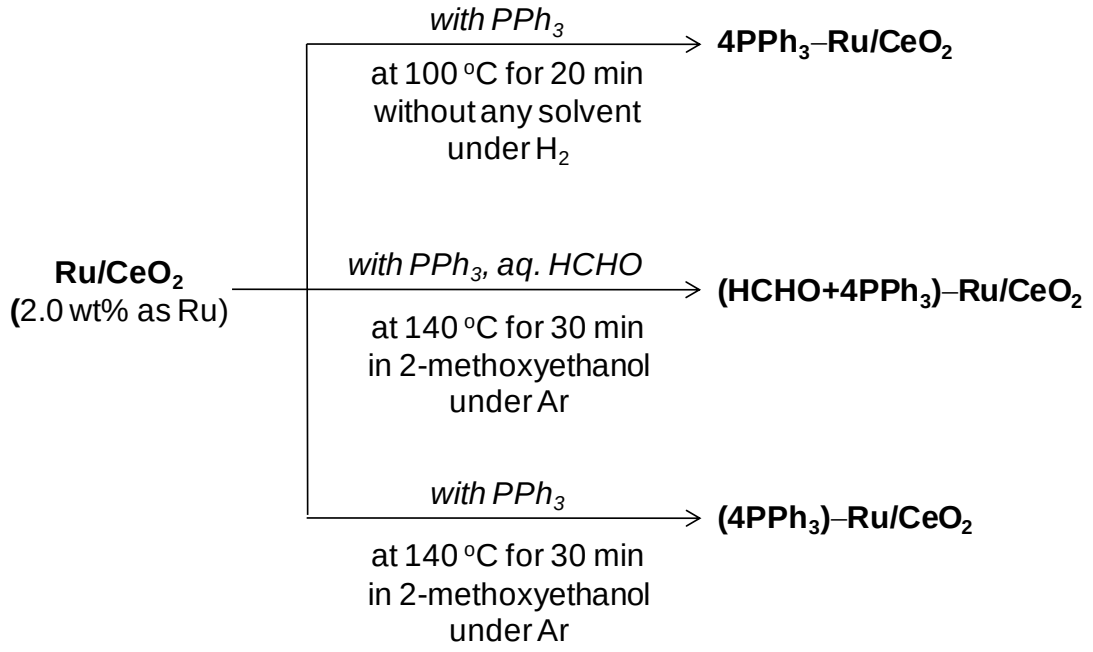
In this chapter, the transformation of Ru(IV)-oxo species on CeO_2 to active Ru

catalysts for the hydroarylation of unsaturated compounds is described. The catalytic system showed much higher efficiency than our previous PPh_3-modified Ru/CeO_2 catalysts, and a variety of unsaturated compounds could be used. Furthermore, the solid Ru catalysts could be easily recycled and used several times without a significant loss of activity.

4.2 Results and discussion

4.2.1 Addition of aromatic C–H bonds to alkenes by modified Ru/CeO_2 catalysts

The methods for the preparation of supported Ru catalysts are summarized in Scheme 1. CeO_2-supported Ru catalysts (Ru/CeO_2) were prepared by impregnation of a solution of $Ru(acac)_3$, followed by calcination in air at 400 °C for 30 min. The Ru/CeO_2 catalyst was then heated at 100 ^oC for 20 min under a hydrogen atmosphere (1 atm) without any solvent in the presence of PPh_3 (4 molar equivalents to Ru) to give a phosphine-modified Ru/CeO_2 catalyst ($4PPh_3$–Ru/CeO_2). On the other hand, Ru/CeO_2 catalysts were treated in 2-methoxyethanol in the presence of PPh_3 with or without formaldehyde (36% aqueous solution; aq. HCHO) at 140 ^oC for 30 min, followed by removal of the solvent under reduced pressure to afford ($HCHO+4PPh_3$)–Ru/CeO_2 or ($4PPh_3$)–Ru/CeO_2, respectively.

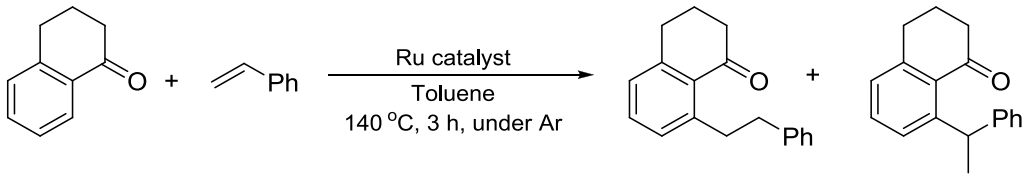


Scheme 1. Method for the preparation of supported Ru catalysts.

As mentioned in chapter 3, the irreversible deposition of siliceous residues derived from vinylsilanes on surface Ru species hampered recycling of the solid catalysts [3c]. Therefore, efforts were made to realize the addition of aromatic C–H bonds with simple unsaturated hydrocarbons. An attempt to add α-tetralone (**1a**) to styrene (**2a**) in the presence of Ru/CeO_2 and PPh_3 (4 equivalents to Ru) resulted in no reaction (Table 1, entry 1). $4PPh_3$–Ru/CeO_2, which showed excellent activity for the addition to triethoxyvinylsilane [3c], also did not show any activity for the reaction of **2a** (entry 2). On the other hand, $(HCHO+4PPh_3)$–Ru/CeO_2 showed excellent activity to give alkylated aromatic ketones **3a** and **4a** in a yield of 85% as a mixture of regioisomers (linear : branch = 3 : 1) (entry 3). In contrast, $(4PPh_3)$–Ru/CeO_2, which was treated in alcohol in the absence of HCHO, was ineffective at all (entry 4). The reaction did not occur with Ru/CeO_2 in the presence PPh_3 and aq. HCHO as external additives (entry 5).

These results indicated that pretreatment in 2-methoxyethanol with aq. HCHO is essential for the transformation of Ru(IV)-oxo species to active Ru catalysts for the hydroarylation of styrene. Other Ru catalysts supported on ZrO_2, SiO_2, Al_2O_3, TiO_2 or MgO treated with PPh_3 and HCHO in 2-methoxyethanol gave no hydroarylation products at all (entries 6–10). Note that the amount of Ru species leached into the solution after the reaction of **1a** with **2a** by (HCHO+4PPh_3)–Ru/CeO_2 catalyst was 7.4% of the Ru species in the fresh catalyst.

Table 1. Hydroarylation of styrene in the presence of supported Ru catalysts[a]



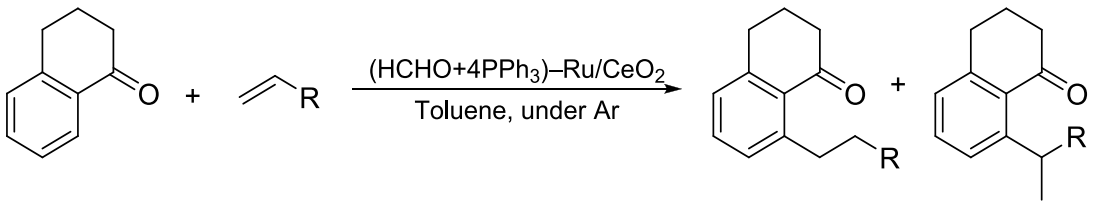
1a **2a** **3aa** **4aa**

Entry	Ru catalyst	Additive	Total yield of **3aa** and 4**aa** (%)[b]	Selectivity (**3aa** : **4aa**)[c]
1	Ru/CeO_2	PPh_3 (0.20 mmol)	0	-
2	$4PPh_3$–Ru/CeO_2	-	0	-
3	$(HCHO+4PPh_3)$–Ru/CeO_2	-	85	75 : 25
4	$(4PPh_3)$–Ru/CeO_2	-	0	-
5	Ru/CeO_2	PPh_3 (0.20 mmol) aq. HCHO (0.50 mL)	0	-
6	$(HCHO+4PPh_3)$–Ru/ZrO_2	-	0	-
7	$(HCHO+4PPh_3)$–Ru/SiO_2	-	0	-
8	$(HCHO+4PPh_3)$–Ru/Al_2O_3	-	0	-
9	$(HCHO+4PPh_3)$–Ru/TiO_2	-	0	-
10	$(HCHO+4PPh_3)$–Ru/MgO	-	0	-

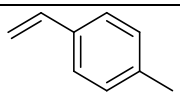
[a] *Reaction conditions*: **1a** (1.0 mmol), **2a** (3.0 mmol), toluene (2.0 mL), Ru catalyst (0.050 mmol as Ru), at 140 °C for 3 h under Ar. [b] Total yield of **3aa** and **4aa** after silica gel chromatography. [c] Molar ratio of isomers determined by ^1H NMR.

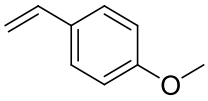
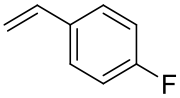
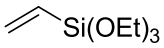
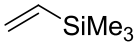
(HCHO+4PPh_3)–Ru/CeO_2 showed high catalytic activity for the hydroarylation of a wide range of alkenes (Table 2). Styrene derivatives **2b**–**2d** efficiently coupled with **1a** to afford alkylated aromatic ketones in high yields. The linear selectivities of the products **3ab**, **3ac** and **3ad** were around 75% (entries 1–3). The catalytic system also showed excellent activities in the reaction of **1a** with vinylsilanes. The reaction of triethoxyvinylsilane (**2e**) went to completion within 30 min (entry 4), although the previous 4PPh_3–Ru/CeO_2 catalysts needed 90 min to finish the reaction. Furthermore, other vinylsilanes without an alkoxy substituent could be used in the present catalytic system and the products **3af** and **3ag** were obtained in excellent yields (entries 5 and 6). Hydroarylation of 2-norbornene (**2h**) also occurred and led to the product in a high yield (entry 7), whereas 1-hexene **2i** was not a good substrate under the present reaction conditions (entry 8).

Table 2. Hydroarylation of alkenes by (HCHO+4PPh_3)–Ru/CeO_2 catalyst.[a]



1a **2** **3** **4**

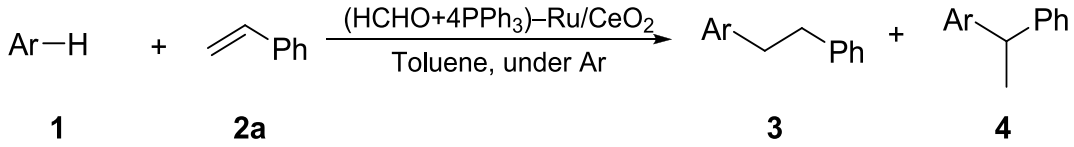
Entry	**2**	Temp. (^oC)	Time (h)	Product	Total yield of **3** and **4** (%)[b]	Selectivity (**3** : **4**)[c]
1	 **2b**	140	3	**3ab**, **4ab**	90	75 : 25

2	 **2c**	140	4	**3ac**, **4ac**	99	74 : 26
3	 **2d**	140	4	**3ad**, **4ad**	94	70 : 30
4[d]	 **2e**	140	0.5	**3ae**	99	100 : 0
5	 **2f**	120	24	**3af**	74	100 : 0
6	 **2g**	140	6	**3ag**	84	100 : 0
7	 **2h**	140	6	**3ah**[e]	78	-
8	 **2i**	140	24	**3ai**	trace	-

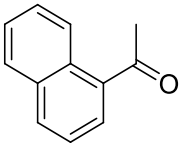
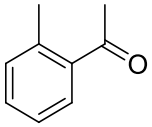
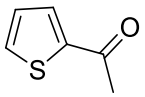
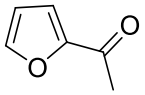
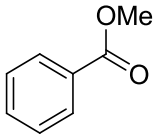
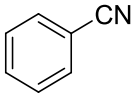
[a] *Reaction conditions*: **1a** (0.50 mmol), **2** (1.5 mmol), toluene (1.0 mL), (HCHO+4PPh$_3$)–Ru/CeO$_2$ catalyst (0.025 mmol as Ru), under Ar. [b] Isolated yield.
[c] Molar ratio of regioisomers determined by ^{1}H NMR. [d] 1.0 mmol of **2e** was used.
[e] Product was obtained as an *exo*-isomer.

The scope of aromatic compounds that could be used in this catalytic system was also examined (Table 3). The addition of aromatic ketones **1b** and **1c** to **2a** took place in the presence of (HCHO+4PPh_3)–Ru/CeO_2 (entries 1 and 2). The reactions of heterocyclic ketones **1d** and **1e** gave the corresponding products **3da** and **3ea** in high yields (entries 3 and 4). However, the present catalytic system was not effective for the addition of aromatic C–H bonds of methyl benzoate or benzonitrile.

Table 3. Addition of aromatic compounds to styrene by (HCHO+4PPh_3)–Ru/CeO_2 catalysts.[a]



1 **2a** **3** **4**

Entry	**1**	Time (h)	Products	Total yield of **3** and **4** (%)[b]	Selectivity (**3** : **4**)[c]
1	 **1b**	3	**3ba**, **4ba**	99	25 : 75
2	 **1c**	24	**3ca**, **4ca**	67	77 : 23
3	 **1d**	3	**3da**, **4da**	98	75 : 25
4	 **1e**	6	**3fa**, **4fa**	75	75 : 25
5	 **1f**	24	**3ha**	trace	-
6	 **1g**	24	**3ia**	0	-

[a]*Reaction conditions*: **1** (0.50 mmol), **2a** (1.5 mmol), toluene (1.0 mL), (HCHO+4PPh_3)–Ru/CeO_2 catalyst (0.025 mmol as Ru), at 140 °C under Ar.
[b] Isolated yield. [c] Molar ratio of isomers determined by ^{1}H NMR.

4.2.2 Characterization of (HCHO+4PPh_3)–Ru/CeO_2 catalysts

To elucidate the state of the active Ru species in the present catalytic system, (HCHO+4PPh_3)–Ru/CeO_2 was characterized by spectroscopic analyses. The diffuse reflectance infrared Fourier transform (DRIFT) spectrum of the Ru/CeO_2 catalyst after treatment with PPh_3 and aq. HCHO is shown in Figure 1. Whereas a peak due to a Ru=O bond was observed at 980 cm^{-1} in the spectrum of Ru/CeO_2 as described in the previous chapters, this peak disappeared in the spectrum of (HCHO+4PPh_3)–Ru/CeO_2. On the other hand, small peaks that could be assigned to Ru-CO or Ru-H species were observed at around 1900–2050 cm^{-1}.

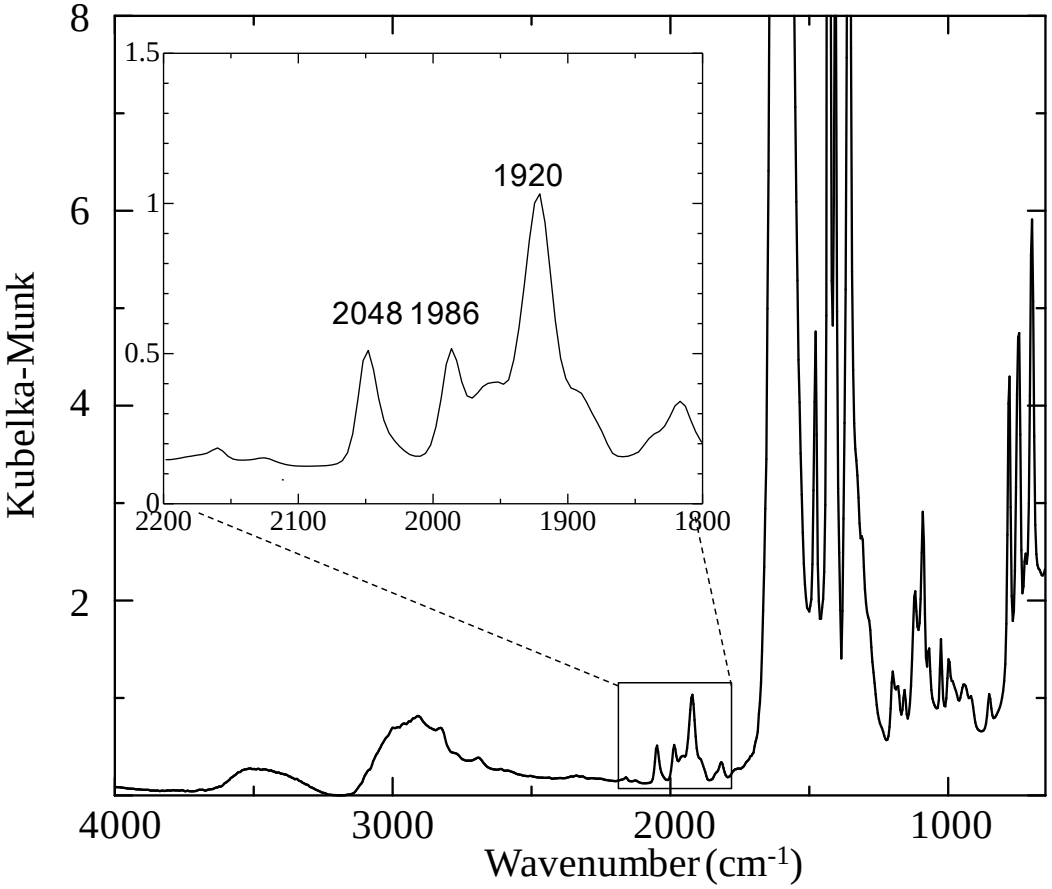


Figure 1. DRIFT spectrum of (HCHO+4PPh_3)–Ru/CeO_2.

Figure 2 shows the X-ray absorption near-edge structure (XANES) spectra of Ru catalysts. The absorption-edge of the (HCHO+4PPh_3)–$RuCeO_2$ catalyst shifted to a lower energy than that of Ru/CeO_2 before treatment and was very close to that of a Ru(II) complex with PPh_3 and CO ligand, whereas the shape of the spectrum was significantly different. This result indicates that the treatment of Ru(IV)=O on CeO_2 with PPh_3 and HCHO in 2-methoxyethanol produced Ru(II) species.

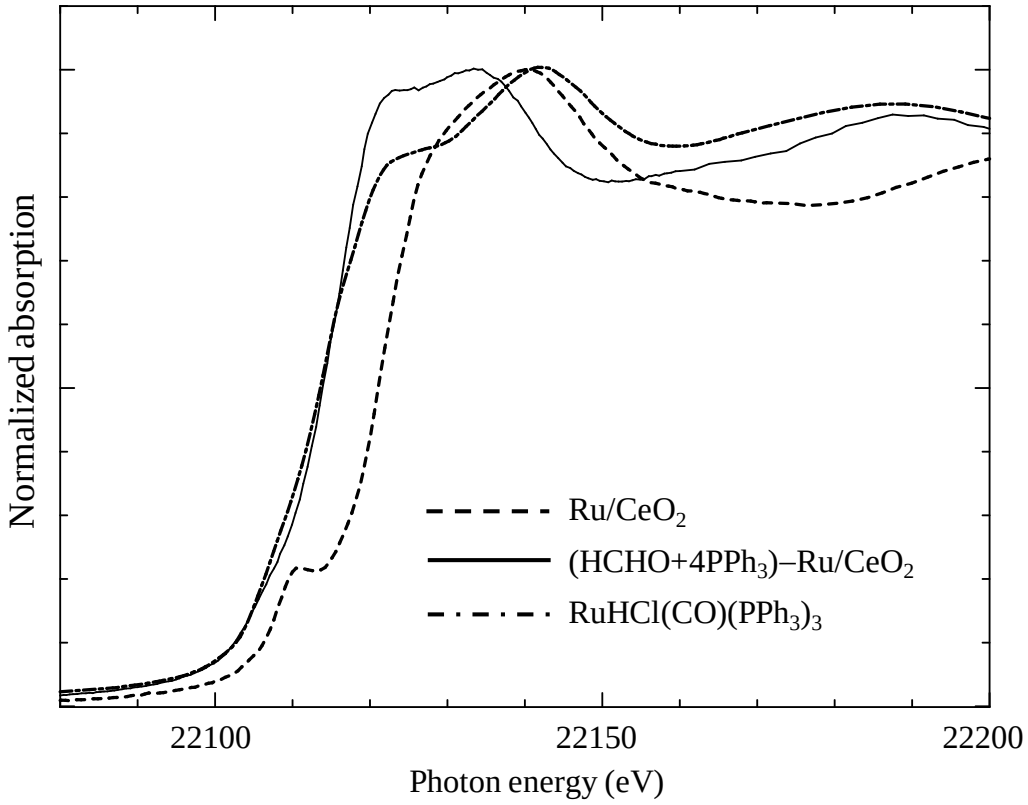
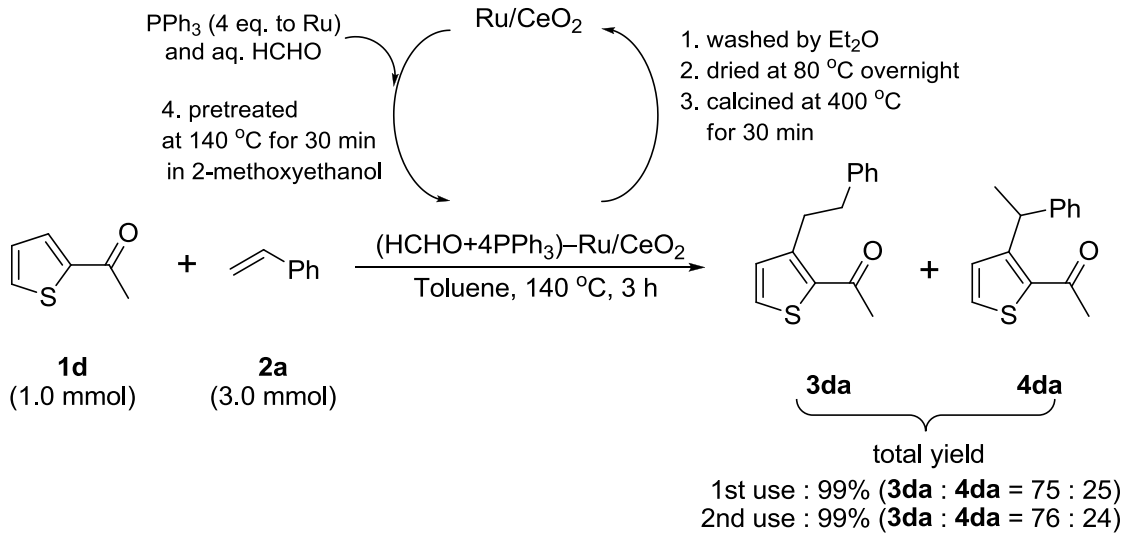


Figure 2. XANES spectra of Ru/CeO_2 before and after the treatment.

A recent mechanistic investigation of the alkylation of aromatic C–H bonds with homogeneous Ru complex catalysts revealed the importance of a CO ligand coordinating active Ru(0) species [7e]. Hiraki et al. reported that the reaction of a low-valent Ru complex with alkoxyvinylsilanes produced Ru-CO species via the oxidative addition of Ru accompanying the cleavage of a Si-O bond of alkoxyvinylsilanes, followed by abstraction of β-hydride from the alkoxo ligand and decarbonylation of the resulting aldehyde [8]. In previous catalytic systems that used untreated Ru/CeO_2 together with PPh_3 or PPh_3–Ru/CeO_2 as catalysts, alkoxyvinylsilanes could act as a source of CO ligand, which might explain the absence of any activity for the reaction of alkenes other than alkoxyvinylsilanes. On the other hand, in the present catalytic system, treatment with PPh_3 and HCHO in alcohol is thought to generate Ru(II) species coordinated by CO and PPh_3, which are transformed, at the initial stage of the reactions, to active Ru(0) species that are effective for the catalytic addition of aromatic C–H bonds to unsaturated carbon–carbon bonds [7c].

4.2.3 Recycling of solid Ru catalysts

One major advantage of solid catalysts is their high recyclability. After the reaction, the present solid Ru catalyst was washed with diethyl ether, dried in air at 80 °C, and then calcined in air at 400 °C to be recovered as Ru/CeO_2. The thus-obtained solid was re-treated with PPh_3 and HCHO in 2-methoxyethanol to give the reproduced $(HCHO+4PPh_3)$–Ru/CeO_2 for the next catalytic run (Scheme 2).

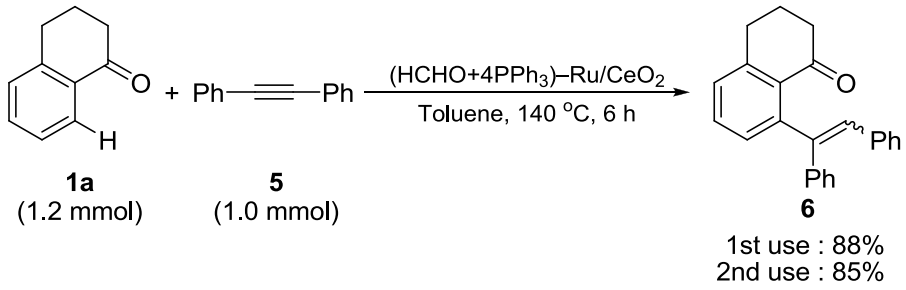


Scheme 2. Recycling of Ru/CeO_2 catalysts.

With the recycled catalysts, the reaction of **1d** with **2a** successfully proceeded to give the corresponding products **3da** and **4da** in a high total yield. Unlike the reaction of vinylsilanes, the surface state of the original Ru/CeO_2 catalysts after the reaction of unsaturated hydrocarbons was restored by washing and re-calcination in air. Thus, the recycled catalysts showed high activities for hydroarylation without a significant loss of activity.

4.2.4 Addition of aromatic C–H bonds to alkyne by utilizing supported Ru catalysts

Multi-substituted alkenes are important organic molecules in material science. Hydroarylation of alkynes is the most atom-economical method for the synthesis of these compounds and a (HCHO+4PPh_3)–Ru/CeO_2 catalyst was found to be effective for the hydroarylation of alkyne (Scheme 3). The reaction of **1a** with diphenylacetylene (**5**) in the presence of a (HCHO+4PPh_3)–Ru/CeO_2 catalyst proceeded efficiently to give triaryl-substituted alkene **6** in 88% yield. Furthermore, the catalyst, recycled by same method as described above, was also effective for the hydroarylation of alkyne **5** to afford **6** in a high yield.



Scheme 3. Hydroarylation of alkyne by (HCHO+4PPh_3)–Ru/CeO_2.

4.3 Conclusions

This chapter described a novel procedure for the generation of highly active and recyclable catalysts that are effective for the addition of aromatic C–H bonds to unsaturated compounds. The treatment of Ru(IV)-oxo species on CeO_2 with PPh_3 and HCHO in 2-methoxyethanol transformed them to active Ru species, which showed high activities for the hydroarylation of various alkenes and alkynes. The present catalytic system is very attractive from practical and environmental points of view because of its simple handling, high recyclability and low contamination of the products by metallic species.

4.4 Experimental

4.4.1 Materials and methods

All manipulations were performed under an argon atmosphere using standard Schlenk techniques. Ruthenium(III) acetylacetonate (Aldrich), all of the aromatic ketones, alkenes and alkynes (TCI) and potassium hydroxide, cerium(III) nitrate hexahydrate, tetrahydrofuran (THF; Wako) were obtained commercially and used without further purification. Ceria was prepared by treating a solution of cerium(III) nitrate hexahydrate (12.6 g, 29 mmol) in 400 mL of deionized water with 40 mL of 3M KOH aqueous solution with stirring for 1 h at room temperature. The resulting precipitates were collected by centrifugation and then dried overnight at 80 ^{o}C. The product was heated in a box furnace at a rate of 10 ^{o}C min^{-1} and maintained at 400 ^{o}C for 30 min to afford ceria in an excellent ceramic yield. Zirconium oxide and magnesium oxide were prepared from zirconium(IV) dinitrate oxide and magnesium nitrate by a method similar to that used to obtain ceria. Titania (JRC-TIO-4), γ-alumina (JRC-ALO-8) and silica (Cabosil) were used as received.

4.4.2 Physical and analytical measurements

The products of catalytic runs were analyzed by GC-MS (Shimadzu GC-MS Parvum 2, Zebron ZB-1 capillary column, i.d. 0.25 mm, length 30 m, at 50–250 ^{o}C) and gas chromatography (GL Sciences GC353, Inertcap 17 capillary column, i.d. 0.25 mm, length 30 m at 50–250 ^{o}C). NMR spectra were recorded on a JEOL JNM-EX-400 (FT, 400 MHz (^{1}H), 100 MHz (^{13}C)) instrument. Chemical shifts (δ) are referenced to $SiMe_4$. The oxide catalysts were analyzed by FTIR and XAFS. Diffuse reflectance IR spectra were recorded using a Nicolet Magna-IR 560 FT-IR spectrometer with DRIFT optical

configuration. Ru K-edge XAFS measurements were performed at BL01B1 beam line at SPring-8 operated at 8 GeV using a Si(311) two-crystal monochromator. XAFS spectra were taken at room temperature. XANES and EXAFS were analyzed using the REX2000 version 2.5 program (Rigaku). Leaching of ruthenium species from the catalysts during the reaction was investigated by ICP atomic emission spectroscopic analysis by using a Shimadzu ICPS-1000III analyzer.

4.4.3 A typical method for the preparation of Ru/Support catalysts

Supported catalysts were prepared by the impregnation method. 1.0 g of a support was added to a solution of $Ru(acac)_3$ (79.5 mg, 0.20 mmol) in 10 mL of THF in air at room temperature. After impregnation, the resulting powder was calcined in air for 30 min to afford the Ru(2.0 wt%)/Support catalyst.

4.4.4 Preparation of $4PPh_3$–Ru/CeO_2

Ru/CeO_2 (125 mg, 0.025 mmol as Ru) was stirred in the presence of PPh_3 (26.3 mg, 0.10 mmol) at 100 ^oC under a hydrogen atmosphere (1 bar) on a hot stirrer with a cooling block for 20 min to give $4PPh_3$–Ru/CeO_2.

4.4.5 Preparation of $(HCHO+4PPh_3)$–Ru/CeO_2 catalyst

Ru/CeO_2 (125 mg, 0.025 mmol as Ru) was stirred in the presence of PPh_3 (26.3 mg, 0.10 mmol) and 36% aq. HCHO (0.25 mL) in 2-methoxyethanol (2 mL) at 140 ^oC under an argon atmosphere on a hot stirrer with a cooling block for 30 min. The resulting solvents and HCHO were removed under reduced pressure at room temperature to give $(HCHO+4PPh_3)$–Ru/CeO_2. The treated catalyst was used for the catalytic reaction

without exposure to open air.

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Chapter 5

Recyclable solid ruthenium catalysts supported on metal oxides for the addition of carboxylic acids to terminal alkynes

5.1 Introduction

Homogeneous catalysts play a significant role in organic syntheses, and can be used to achieve excellent yields and/or control the selectivity through the choice of suitable ligands and additives. However, they are often associated with practical and environmental disadvantages, and the use of heterogeneous catalysts, particularly solid oxide catalysts, is an attractive alternative to overcome these drawbacks, as discussed in General Introduction.

On the other hand, vinyl esters are important reactants and useful intermediates for many organic reactions because of their numerous industrial applications [1–8], and the addition of carboxylic acids to alkynes has been shown to be an atom-economical route to vinyl esters [9,10]. Low-valent ruthenium complexes have been reported to act as excellent homogeneous catalysts for this reaction [11–18]. Whereas the activities of ruthenium complex catalysts immobilized onto phosphine-modified resin [19a] as well as related Pd [19b] and Au [19c] catalysts for analogous reactions have been reported, there have been no previous reports on the application of solid oxide-supported ruthenium catalysts. In the previous chapters, Ru/CeO_2 have been found to be effective

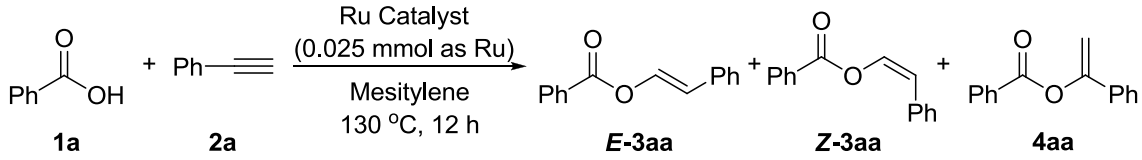
for various synthetic reactions [20,21]. These results suggest that an Ru/CeO_2 catalyst may be a good alternative to homogeneous ruthenium catalysts.

In this chapter, solid oxide-supported ruthenium catalysts that are effective for the synthesis of vinyl esters by the addition of carboxylic acids to terminal alkynes is described. Simple catalysts, Ru/CeO_2 and Ru/ZrO_2, showed excellent activities and could be used for the reactions of a variety of substrates. These catalysts were recyclable without a significant loss of activity, and the leaching of ruthenium species was not observed after cooling the reaction mixture. The effects of ruthenium precursors were examined and the catalysts were characterized by spectroscopic techniques.

5.2 Results and discussion

The reaction of benzoic acid **1a** with ethynylbenzene **2a** at 130 ^{o}C for 12 h in the presence of a catalytic amount of Ru/CeO_2 afforded adducts in an excellent total yield of 96% (entry 1 in Table 1). The Ru/CeO_2 catalysts were prepared by the impregnation of [$RuCl_2$(*p*-cymene)]$_2$ on cerium oxide followed by calcination at 400 ^{o}C. The major product of the reaction was the *E*-isomer of the anti-Markovnikov adducts (*E*-**3aa**), with 74% selectivity, and was obtained together with the *Z*-isomer (*Z*-**3aa**) and a small amount of the Markovnikov adduct **4aa**. There was no sign of dimers or oligomers of **2a**. The reaction at 120 ^{o}C afforded the adducts in a lower total yield (entry 2). The reaction proceeded even in the open air, whereas the yield of the products was moderate (entry 3). The activity of the present solid catalyst is comparable to that of a homogeneous ruthenium carbonyl catalyst [12a]. Under the present conditions, the reaction catalyzed by $Ru_3(CO)_{12}$ afforded the vinyl esters in a total yield of 77% with 73% selectivity for *E*-**3aa** (entry 9). [$RuCl_2$ (*p*-cymene)]$_2$, the precursor of the supported Ru catalysts, showed a lower activity (entry 10), whereas several homogeneous ruthenium complex catalysts bearing phosphorus ligands [13–18,22] have been reported to show excellent activities at lower temperatures. The activity of the catalysts was significantly affected by the catalyst support (entries 4–8). The ZrO_2-supported catalyst showed activity comparable to that of the CeO_2-supported catalyst. The other ruthenium catalysts supported on Al_2O_3, TiO_2, SiO_2, or MgO were not effective. Note that a similar trend was observed in the C–C bond-forming reactions with supported Ru catalysts, as described in the previous chapters.

Table 1. Activity of ruthenium catalysts for the addition of benzoic acid **1a** to ethynylbenzene **2a**.[a]



Entry	Catalyst	Total yield (%)[b]	Selectivity (%)[c] (*E*-**3aa** : *Z*-**3aa** : **4aa**)
1	Ru/CeO_2	96	74 : 21 : 5
2[d]	Ru/CeO_2	69	74 : 20 : 6
3[e]	Ru/CeO_2	46	65 : 33 : 2
4	Ru/ZrO_2	94	73 : 21 : 6
5	Ru/Al_2O_3	8	75 : 25 : 0
6	Ru/TiO_2	7	71 : 29 : 0
7	Ru/SiO_2	trace	—
8	Ru/MgO	trace	—
9	$Ru_3(CO)_{12}$[f]	77	73 : 19 : 8
10	$[RuCl_2(p\text{-cymene})]_2$[f]	54	52 : 43 : 5

[a] *Reaction conditions*: **1a** (1.0 mmol), **2a** (1.3 mmol), mesitylene (1.0 mL), Ru/CeO_2 catalyst (0.025 mmol as Ru), at 130 °C for 12 h. [b] Total yield of *E*-**3aa**, *Z*-**3aa** and **4aa** determined by GLC. [c] Molar ratio of isomers determined by GLC. [d] At 120 °C.
[e] Reaction under the air atmosphere. [f] Homogeneous catalyst.

As shown in Table 2, the activity of Ru/CeO_2 catalysts was markedly affected by the ruthenium precursors used for their preparation. In general, catalysts prepared from precursors with chloride ligands showed high activities. However, the ruthenium precursors did not influence the selectivity. Among the precursors examined, $[RuCl_2(p\text{-cymene})]_2$ was found to be most suitable. The Ru/CeO_2 catalyst prepared from $Ru_3(CO)_{12}$ which has no chloride ligands showed low activity, but the addition of ammonium chloride (10 equivalents to Ru) to the reaction mixture gave a higher activity than the catalyst without NH_4Cl (entries 5 and 6). This result clearly indicates that the chloride species has a promoting effect. Catalysts prepared from $[RuCl_2(p\text{-cymene})]_2$ were used in the following study.

Table 2. Effect of ruthenium precursors of Ru/CeO_2 catalysts.[a]

Entry	Precursor	Total yield (%)[b]	Selectivity (%)[c] (*E*-**3aa** : *Z*-**3aa** : **4aa**)
1	$[RuCl_2(p\text{-cymene})]_2$	96	74 : 21 : 5
2	$RuCl_3 \cdot nH_2O$	91	73 : 22 : 5
3	$[RuCl_2(CO)_3]_2$	72	72 : 22 : 6
4	$Ru(acac)_3$	20	70 : 25 : 5
5	$Ru_3(CO)_{12}$	14	64 : 29 : 7
6	$Ru_3(CO)_{12}$[d]	43	65 : 26 : 9

[a] *Reaction conditions:* **1a** (1.0 mmol), **2a** (1.3 mmol), mesitylene (1.0 mL), Ru/CeO_2 catalyst (0.025 mmol as Ru), at 130 °C for 12 h. [b] Total yield of *E*-**3aa**, *Z*-**3aa** and **4aa** determined by GLC. [c] Molar ratio of isomers determined by GLC.
[d] NH_4Cl (10 eq. to Ru) was added to the reaction mixture.

The effects of ruthenium precursors on the surface composition of the fresh catalysts were examined by XPS. As shown in Table 3, residual chloride species were observed on the surface of the catalysts prepared using Cl-containing ruthenium complexes, while there were no significant differences in the atomic ratios of the surface ruthenium species. The Ru $3d_{5/2}$ binding energies of these catalysts indicated the presence of surface Ru(IV) species [23], but the electronic effects of Cl species were not distinctly recognized.

Table 3. XPS analysis of Ru/CeO_2 catalysts prepared from various precursors.[a]

Precursors	Surface concentration (atomic %)					Ru $3d_{5/2}$ (eV)
	C	Ru	Cl	Ce	O	
$[RuCl_2(p\text{-cymene})]_2$	12.00	1.37	3.71	28.77	54.15	281.93
$RuCl_3 \cdot nH_2O$	17.39	1.21	3.70	26.34	51.36	281.63
$[RuCl_2(CO)_3]_2$	17.50	1.29	3.34	25.73	52.14	281.73
$Ru_3(CO)_{12}$	20.13	1.36	trace	24.80	53.71	281.61
$Ru(acac)_3$	17.50	1.34	trace	26.41	54.75	281.53

[a] Measured at -100 ^oC.

To investigate whether the reaction proceeded on the surface of the solid catalyst [24,25], the effect of removal of the catalysts by hot filtration through a PTFE filter (pore size 0.45 nm) was examined. Figure 1 shows the time course of the reaction of **1a** with **2a** at 130 ^{o}C. Formation of the vinyl esters was greatly suppressed, but not completely stopped by removal of the solid catalyst. Note that ruthenium species was not detected in the cold filtrate after the reaction at 130 ^{o}C for 12 h by ICP-AES. These results indicate that the reaction basically requires the presence of the solid catalyst. The ceria support might act as a macroligand that stabilizes and/or holds the catalytically active ruthenium species. However, the contribution of soluble ruthenium species or nano-sized ruthenium colloids, which passed through the filter, could not be completely ruled out.

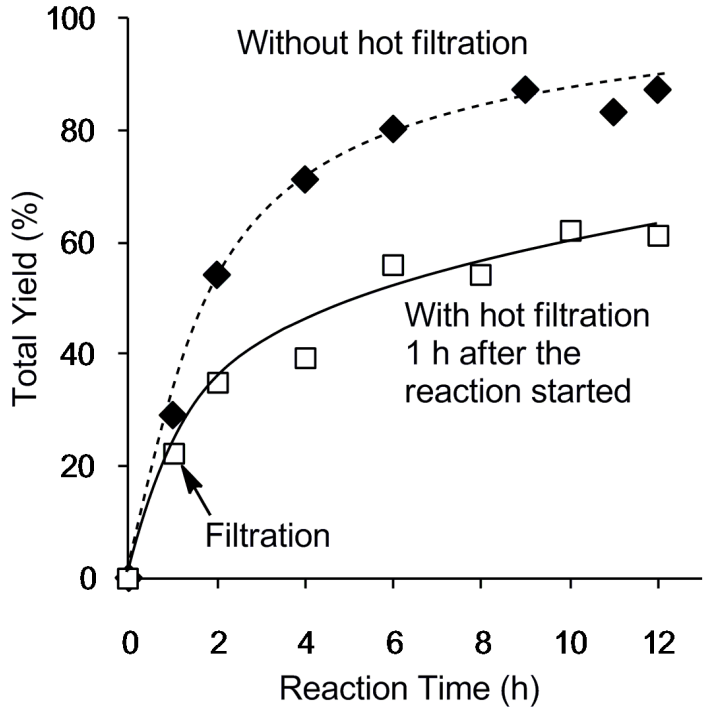
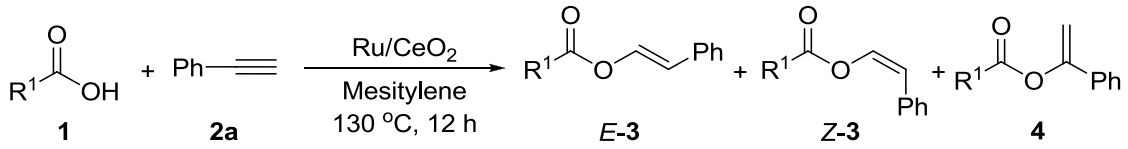


Figure 1. Effects of catalyst removal by hot filtration on the reaction of **1a** with **2a** at 130 °C. The reaction conditions were identical to those for entry 1 in Table 1.

The Ru/CeO_2 catalyst could be used with a variety of substrates. The results of the reaction of various carboxylic acids **1b–i** with **2a** at 130 ^{o}C for 12 h are shown in Table 4. The reaction with aromatic carboxylic acids with both electron-donating and electron-withdrawing substituents (**1b**–**e**) proceeded smoothly to afford adducts in moderate to high yields. A bulky substrate (**1f**) and carboxylic acids with thiophene and furan rings (**1g** and **1h**) were also applicable. The reaction with an aliphatic carboxylic acid (**1i**) also gave the desired adduct in a moderate yield. In all of the cases examined, the major products were *E*-isomers of anti-Markovnikov adducts.

Table 4. Scope of substrates (carboxylic acids).[a]

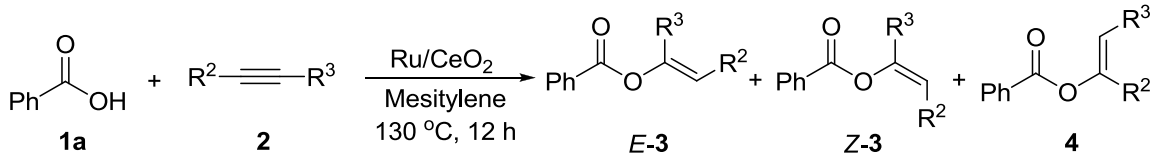


Entry	**1**	R^1	Total yield (%)[b]	Selectivity (%)[c] (*E*-**3** : *Z*-**3** : **4**)
1	**1b**	4-$CH_3C_6H_4$	58	79 : 17 : 4
2	**1c**	3-MeO-C_6H_4	90	76 : 18 : 6
3	**1d**	3-NO_2-C_6H_4	87	48 : 34 : 18
4	**1e**	4-CF_3-C_6H_4	82	66 : 24 : 10
5	**1f**	2,4,6-$(CH_3)_3C_6H_2$	92	71 : 27 : 2
6	**1g**	2-thienyl	81	56 : 38 : 6
7	**1h**	3-furyl	76	72 : 22 : 6
8	**1i**	*n*-C_7H_{15}	40	75 : 21 : 4

[a] *Reaction conditions*: **1** (1.0 mmol), **2a** (1.3 mmol), mesitylene (1.0 mL), Ru/CeO_2 catalyst (0.025 mmol as Ru), at 130 °C for 12 h. [b] Isolated yield. [c] Molar ratio of isomers determined by ^{1}H NMR.

The reactions with **1a** and various alkynes **2** were examined. As shown in Table 5, the reactions of terminal alkynes with phenyl groups (**2b** and **2c**) and that with a thiophene ring (**2d**) afforded the adducts in high yields, while the reaction with 2-ethynylpyridine (**2e**) resulted in a low yield of vinyl esters. The selectivity greatly depended on the alkynes. High selectivity of a Markovnikov adduct (**4**) was observed with an alkyne bearing a pyridyl group (**2e**). On the other hand, the reactions of a terminal alkyne with a trimethylsilyl substituent (**2f**) and internal alkynes (**2g** and **2h**) did not proceed under the present conditions.

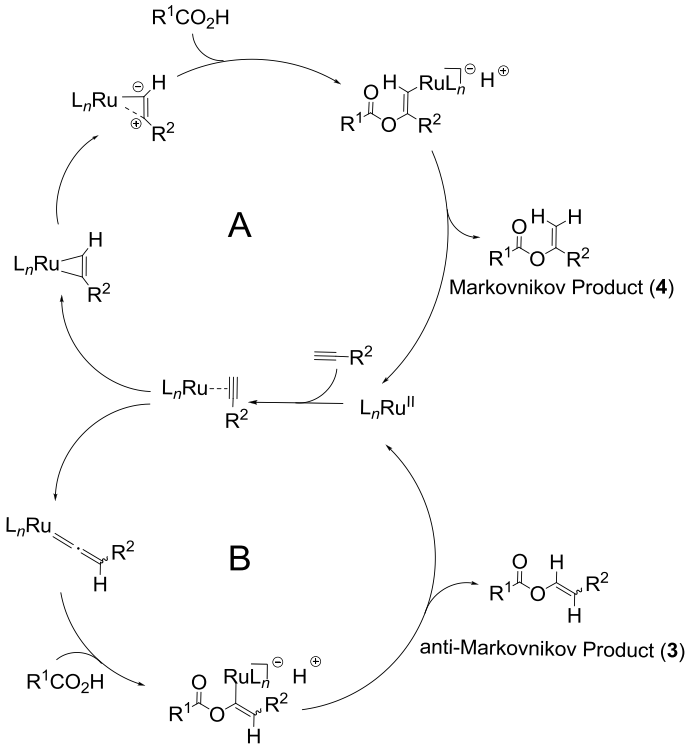
Table 5. Scope of substrates (alkynes).[a]



Entry	**2**	R^2	R^3	Total yield (%)[b]	Selectivity (%)[c] (*E*-**3** : *Z*-**3** : **4**)
1	**2b**	4-$CH_3C_6H_4$	H	83	67 : 23 : 10
2	**2c**	4-MeO-C_6H_4	H	72	44 : 17 : 39
3	**2d**	3-thienyl	H	78	59 : 17 : 24
4	**2e**	2-pyridyl	H	24	43 : 0 : 57
5	**2f**	$(CH_3)_3Si$	H	trace	—
6	**2g**	*n*-C_3H_7	*n*-C_3H_7	0	—
7	**2h**	Ph	Ph	0	—

[a] *Reaction conditions*: **1a** (1.0 mmol), alkyne **2** (1.3 mmol), mesitylene (1.0 mL), Ru/CeO_2 catalyst (0.025 mmol as Ru), at 130 °C for 12 h. [b] Isolated yield. [c] Molar ratio of isomers determined by ^1H NMR.

To date, several mechanisms have been proposed for homogeneously catalyzed reactions (Scheme 1) [9,18b]. One plausible mechanism involves the formation of vinylidene intermediates (cycle B) [16b,17b], while another probable cycle is likely to start with the coordination of an alkyne to a ruthenium species, followed by the addition of a carboxylate nucleophile to the η^2-coordinated alkyne (cycle A) [16b]. We examined the reaction of **1a** with PhC≡CD (**2a**-d_1), and the deuterium shifting from the terminal to the 2-position was found to be predominant, which supported the formation of the ruthenium vinylidene species as an intermediate (cycle B). In entry 4 of Table 5 (the reaction of **1a** with **2e**), the strong coordination of a pyridyl group to a ruthenium center would promote the formation of a η^2-alkyne intermediate, which leads to a Markovnikov product through cycle A.



Scheme 1. Proposed catalytic mechanisms for the addition of carboxylic acids to terminal alkynes. *Cycle A:* Markovnikov addition; *Cycle B:* anti-Markovnikov addition.

One major advantage of heterogeneous catalysts is their reusability. Therefore, the changes in the activity of Ru/CeO_2 catalyst over the course of repeated uses were examined, as shown in Table 6. After the first run, which gave the adducts in 96% yield, the catalyst was recovered from the reaction mixture by centrifugation followed by washing three times with diethyl ether (10 mL) at room temperature, and then calcined at 400 °C for 30 min in air. The recovered Ru/CeO_2 catalyst gave the adducts in 93% yield in the 2nd use, although the yields decreased to some extent in the 3rd and 4th uses. Reuse of the catalyst without calcination resulted in a significant decrease in catalytic activity. The severe deposition of organic species on the surface would suppress the activity of the catalyst.

Table 6. Activities of fresh and reused Ru/CeO_2 catalysts.[a]

Treatment of recovered catalyst	Catalyst	Total yield (%)[b]	Selectivity (%)[c] (*E*-**3aa** : *Z*-**3aa** : **4aa**)
	Fresh[d]	96	74 : 21 : 5
Washing + drying + calcination	2nd use	93	75 : 20 : 5
	3rd use	72	72 : 21 : 7
	4th use	71	72 : 23 : 5
	4th use[e]	82	73 : 22 : 5
Washing + drying	2nd use	79	72 : 23 : 5
	3rd use	43	70 : 23 : 7
	4th use	28	71 : 22 : 7

[a] *Reaction conditions:* **1a** (1.0 mmol), **2a** (1.3 mmol), mesitylene (1.0 mL), Ru/CeO_2 catalyst (0.025 mmol as Ru) prepared from $[RuCl_2(p\text{-cymene})]_2$, at 130 °C for 12 h. [b] Total yield of *E*-**3aa,** *Z*-**3aa** and **4aa** determined by GLC. [c] Molar ratio of isomers determined by GLC. [d] Entry 1 in Table 1. [e] Reaction time, 18 h.

To examine the properties of the Ru/CeO_2 catalyst before and after the reaction, H_2 temperature-programmed reduction (TPR) measurements were performed, as shown in Figure 2. In the profile of the fresh catalyst, two peaks appeared at a low-temperature range, one at *ca*. 50 °C and one at 75 °C. The reduction of ruthenium species on other supports such as titania occurred at a temperature higher than 200 °C, and a temperature higher than 100 °C was required for the reduction of bulk RuO_2 [20,26]. These results indicate that the surface ruthenium species on ceria is easily reduced. The used catalyst after the calcination showed a profile similar to that of the fresh catalyst, suggesting that the original surface ruthenium species are regenerated by calcination of the used catalyst.

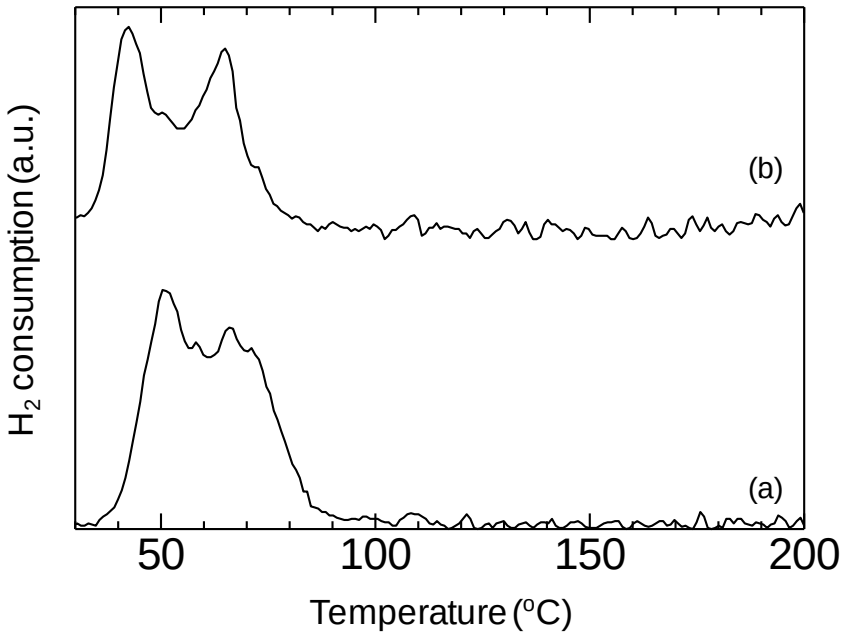


Figure 2. H_2 TPR profiles of (a) fresh and (b) used Ru(2.0 wt%)/CeO_2 catalyst prepared from $[RuCl_2(p\text{-cymene})]_2$. The used catalyst was calcined in air at 400 °C for 30 min.

The surface states of the Ru/CeO_2 catalyst before and after the reaction were also examined by XPS, DRIFTS, and TG. According to the XPS results shown in Table 7, a large part of the surface of the used catalyst was covered by carbonaceous materials, probably because of the deposition of benzoate species on the surface during the catalytic run, as suggested by DRIFTS (deta was not shown). TG analysis of the catalyst after the first use showed *ca.* 4 wt% weight decrease due to the combustion of organic species adsorbed on the surface. Unfortunately, severe overlapping with C 1*s* peaks disturbed the precise measurement of the Ru $3d_{5/2}$ binding energy of the used catalyst. Most of the carbonaceous species was removed by calcination at 400 °C for 30 min in air. The surface atomic ratio of Cl greatly decreased after the 1st use, indicating that some of the chloride species were leached from the surface during the catalytic run. A slight decrease in the surface ruthenium ratio of the used catalyst after calcination can be attributed to the sintering of ruthenium species during the regeneration procedure, since the leaching of ruthenium species was not observed after cold filtration of the catalyst.

Table 7. XPS analysis of the Ru(2.0 wt%)/CeO_2 catalyst prepared from $[RuCl_2(p\text{-cymene})]_2$.[a]

Remarks	Surface concentration (atomic %)					Ru $3d_{5/2}$ (eV)
	C	Ru	Cl	Ce	O	
fresh catalyst	12.00	1.37	3.71	28.77	54.15	281. 93
after 1st use	40.62	1.02	1.90	15.81	40.65	—
after 1st use, calcined	12.35	1.10	2.84	24.12	59.60	281.23

[a] Measured at -100 °C.

Figure 3 shows DRIFT spectra of the Ru/CeO_2 catalyst in the range of 800 to 1100 cm^{-1} before and after the catalytic run (entry 1 of Table 1). The spectrum of the fresh catalyst showed a distinct band at 984 cm^{-1} that could be assigned to a ruthenium oxo (Ru=O) species [26]. Although such a distinct peak was not recognized for Ru/ZrO_2, the formation of similar ruthenium–oxygen species has also been proposed for the the zirconia-supported catalyst [27]. There were no signs of oxo species for ruthenium catalysts supported on Al_2O_3, TiO_2, SiO_2, or MgO. The characteristic band at 984 cm^{-1} of Ru/CeO_2 disappeared after the reaction (Fig. 3(c)), suggesting that the ruthenium oxo species were transformed to other catalytically active species during the reaction. The band at 980 cm^{-1} reappeared in the spectrum of the used catalyst after calcination, indicating that ruthenium oxo species were regenerated (Fig. 3(d)).

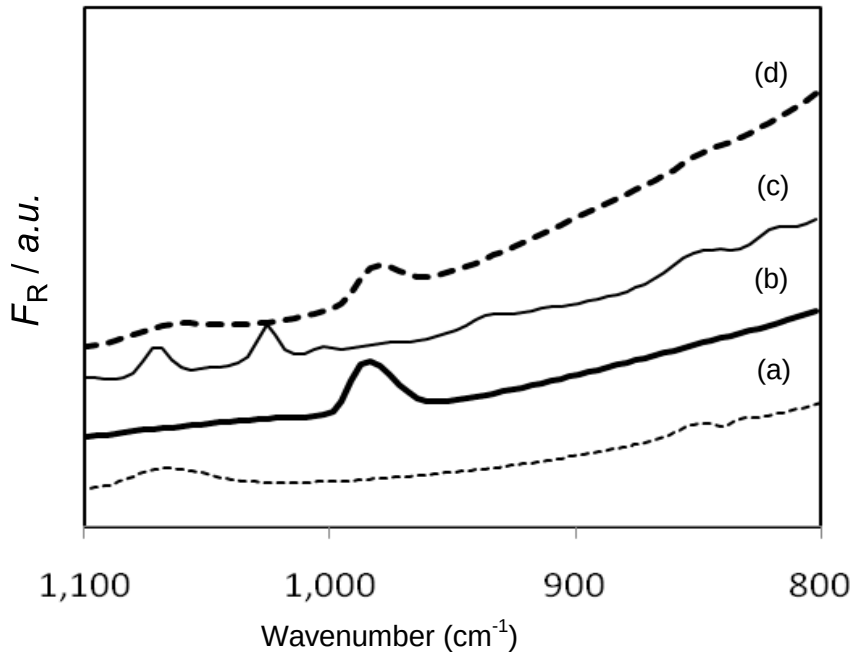


Figure 3. DRIFT spectra of (a) CeO_2, (b) fresh Ru/CeO_2 catalyst prepared from $[RuCl_2(p\text{-cymene})]_2$, (c) used catalyst, and (d) used catalyst after calcination.

5.3 Conclusions

In this chapter, solid oxide-supported ruthenium catalysts that are effective for the addition of a variety of carboxylic acids to terminal alkynes are described: Ru/CeO_2 and Ru/ZrO_2 showed excellent activities. A variety of carboxylic acids and terminal alkynes could be used with this catalyst. The present Ru/CeO_2 catalyst was recyclable, and the leaching of ruthenium species was not observed after the reaction. These features are quite attractive and advantageous from synthetic, industrial, and environmental points of view.

5.4 Experimental

5.4.1 Materials and methods

All manipulations were performed under an argon atmosphere using standard Schlenk techniques. Di-μ-chlorobis[(*p*-cymene)chlororuthenium(II)] (Strem Chemicals), dodecacarbonyltriruthenium (Strem Chemicals), ruthenium trichloride *n*-hydrate (Tanaka Kikinzoku Kogyo), ruthenium(III) acetylacetonate (Aldrich), dichlorotricarbonylruthenium(II)dimer (Strem Chemicals), cerium(III) nitrate hexahydrate (Wako), zirconium oxynitrate (Nakalai Tesque), magnesium nitrate hexahydrate (Wako), aqueous ammonia solution (28%, Nacalai Tesque), biphenyl (Wako), benzoic acid (Nacalai Tesque), ethynylbenzene (TCI), ammonium chloride (Nacalai Tesque), *p*-toluic acid (TCI), *m*-anisic acid (TCI), 3-nitrobenzoic acid (TCI), α,α,α-trifluoro-*p*-toluic acid (Aldrich), 2,4,6-trimethylbenzoic acid (TCI), 2-thiophenecarboxylic acid (Wako), 3-furancarboxylic acid (Wako), octanoic acid (Wako), *p*-ethynyltoluene (Wako), 4-ethynylanisole (Aldrich), 3-ethynylthiophene (Aldrich), 2-ethynylpyridine (Wako), trimethylsilylacetylene (TCI), 4-octyne (Wako), diphenylacetylene (Aldrich), mesitylene (Nacalai Tesque), diethyl ether (Nacalai Tesque), methanol (Wako), tetrahydrofuran (Wako), hexane (Nacalai Tesque), ethyl acetate (Nacalai Tesque), phenylacetylene-d_1 (Isotech), chloroform-*d* (Acros Organics), and dichloromethane-d_2 (Acros Organics) were obtained commercially and used without further purification. Cerium oxide was prepared by the treatment of a solution of cerium(III) nitrate hexahydrate (12.6 g, 29 mmol) in 400 mL of deionized water with 38 mL of 28% aqueous ammonia with stirring for 1 h at room temperature. The resulting precipitate was collected by centrifugation, and then air-died at 80 °C overnight. The product was heated in a box furnace at a rate of 10 °C min^{-1} and

maintained at 400 °C for 30 min to afford ceria in excellent ceramic yield. Zirconium oxide and magnesium oxide were prepared by the same method using zirconium oxynitrate and magnesium nitrate hexahydrate, respectively. Titanium oxide (JRC-TIO-8), γ-alumina (JRC-ALO-8), and silica (CAB-O-SIL) were used as received.

5.4.2 Characterization

NMR spectra were recorded on a JEOL JNM-EX-400 (FT, 400 MHz (^{1}H)) instrument. Chemical shifts (δ) are referenced to $SiMe_4$. High-resolution mass spectra (FAB) were recorded on a JEOL SX102A spectrometer with *m*-nitrobenzyl alcohol as a matrix. The oxide catalysts were analyzed by XPS, DRIFT, H_2-TPR, and TG-DTA. X-ray photoelectron spectra (XPS) of the catalysts were acquired using an ULVAC-PHI 5500MT system equipped with a hemispherical energy analyzer. Samples were mounted on indium foil and then transferred to the XPS analyzer chamber. The residual gas pressure in the chamber during data acquisition was less than 1×10^{-8} Torr (1 Torr = 133.3 N m^{-2}). The spectra were measured at *ca*. -100 °C by Mg *K*α radiation (15 kV, 400 W). The electron take-off angle was set at 45 deg. Binding energies were referenced to the C 1s level of residual graphitic carbon [23]. Diffuse reflectance infrared Fourier transform (DRIFT) spectroscopy was carried out using a Nicolet Magna-IR 560 FT-IR spectrometer with a DRIFT optical configuration. Temperature-programmed reduction (TPR) was carried out with a flow-type reactor. Hydrogen (1.9 vol.%) in Ar was passed at 30 cm^3 min^{-1} under atmospheric pressure through a reaction tube containing 50 mg of the catalysts. The tube was heated with an electric furnace at 2 °C min^{-1}, and the amount of H_2 consumed was monitored with a TC detector of a Shimadzu 4CPT gas chromatograph. Thermogravimetry (TG) and differential thermal analysis (DTA) were

performed using a Rigaku TG8120 system. The sample (*ca*. 5 mg) was heated at a rate of 10 °C min^{-1} in an air flow (50 mL min^{-1}). The leaching of ruthenium species from the catalysts during the reaction was investigated by the inductively coupled plasma-atomic emission spectroscopy (ICP-AES) using a Shimadzu ICPS-1000III analyzer. The products of catalytic runs were analyzed by GC-MS (Shimadzu GC-MS Parvum 2; Zebron ZB-1 capillary column, i.d. 0.25 mm, length 30 m, at 50−250 °C) and gas-liquid chromatography (GL Sciences GC353; Inertcap 17 capillary column, i.d. 0.25 mm, length 30 m at 50−250 ^{o}C).

5.4.3 Preparation of the Ru/CeO_2 catalysts

Supported catalysts were prepared by the impregnation method through the use of various supports and ruthenium complexes. A typical procedure is as follows: 1.0 g of CeO_2 was added to a solution of $[RuCl_2(p\text{-cymene})]_2$ (62 mg, 0.10 mmol, 20 mg as Ru) in 10 mL of methanol at 50 °C. After impregnation, the resulting light yellow powder was calcined in air at 400 °C for 30 min to afford Ru(2.0 wt%)/CeO_2 as a dark brown powder.

5.4.4 General procedure for the addition of carboxylic acids to terminal alkynes

All of the reactions were performed by the use of hot stirrers equipped with cooling blocks for refluxing the solution. A typical reaction procedure is as follows: A mixture of carboxylic acid (1.0 mmol) and terminal alkyne (1.3 mmol) in mesitylene (1.0 mL) was placed in a 20 mL glass Schlenk tube with a balloon under an Ar atmosphere together with 125 mg of the Ru(2.0wt%)/CeO_2 catalyst (0.025 mmol as Ru). The reaction mixture was stirred at 130 °C for 12 h, and then cooled rapidly in an ice

bath. The products were identified by GC-MS, ^{1}H and ^{13}C NMR, and quantified by ^{1}H NMR and GLC analyses using biphenyl as an internal standard.

5.4.5 Hot filtration test

A 20 mL Schlenk tube was charged with benzoic acid (**1a**, 122 mg, 1.0 mmol), ethynylbenzene (**2a**, 0.15 mL, 1.3 mmol), mesitylene (1.0 mL), and 125 mg of the Ru(2.0 wt%)/CeO_2 catalyst (0.025 mmol as Ru) together with an internal standard (biphenyl, *ca*. 46 mg) under an argon atmosphere. After the reaction was allowed to proceed for 1 h at 130 °C, the mixture was filtered through a 0.45 μm syringe filter (Millipore Millex LH) into another preheated Schlenk tube. The filtrate was stirred at 130 °C, and the conversion and yields of the product after filtration were followed by GC and GC-MS analyses.

5.4.6 Characterization of products

Styryl 4-methylbenzoate (*E*-3ba, ***Z*-3ba** and **4ba):** Light brown oil. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ, *E*-isomer (***E*-3ba**): 8.09 (d, *J* = 12.6 Hz, 1H), 8.03–7.23 (m, 9H), 6.58 (d, *J* = 12.6 Hz, 1H), 2,44 (s, 3H). *Z*-isomer (***Z*-3ba**): 5.84 (d, *J* = 7.6 Hz, 1H), 2,45 (s, 3H), other peaks were overlapped with those of the other isomers. Markovnikov adduct (1-phenylvinyl 3-nitrobenzoate, **4ba**): 5.59 (d, *J* = 2.0 Hz, 1H), 5.15 (d, *J* = 2.0 Hz, 1H), other peaks were overlapped with those of the other isomers. HRMS: Calculated for $C_{16}H_{14}O_2$ (M): 238.0994; found: 238.0999.

Styryl 3-methoxybenzoate (*E*-3ca, ***Z*-3ca** and **4ca):** Light brown oil. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ, *E*-isomer (***E*-3ca**): 8.09 (d, *J* = 12.6 Hz, 1H), 7.78–7.15 (m, 9H), 6.59 (d, *J* = 12.6 Hz, 1H), 3.88 (s, 3H). *Z*-isomer (***Z*-3ca**): 5.86 (d, *J* = 7.2 Hz, 1H), other peaks were overlapped with those of the other isomers. Markovnikov adduct (1-phenylvinyl 3-methoxybenzoate, **4ca**): 5.59 (d, *J* = 2.0 Hz, 1H), 5.16 (d, *J* = 2.0 Hz, 1H), other peaks were overlapped with those of the other isomers. HRMS: Calculated for $C_{16}H_{15}O_3$ (M+H): 255.1021; found: 255.1014.

Styryl 3-nitrobenzoate (*E*-3da, ***Z*-3da** and **4da):** Yellowish white solid. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ, *E*-isomer (***E*-3da**): 9.00 (t, *J* = 1.0 Hz, 1H), 8.51–8.46 (m, 2H), 8.08 (d, *J* = 12.8 Hz, 1H), 7.78–7.15 (m, 6H), 6.69 (d, *J* = 12.8 Hz, 1H). *Z*-isomer (***Z*-3da**): 9.02 (m, 1H), 5.96 (d, *J* = 7.2 Hz, 1H), other peaks were overlapped with those of the other isomers. Markovnikov adduct (1-phenylvinyl 3-nitrobenzoate, **4da**): 5.62 (d, *J* = 2.4 Hz, 1H), 5.21 (d, *J* = 2.4 Hz, 1H), other peaks were overlapped with those of the other isomers. HRMS: Calculated for $C_{15}H_{11}NO_4$ (M): 269.0688; found: 269.0692.

Styryl 4-(trifluoromethyl)benzoate (*E*-3ea, ***Z*-3ea** and **4ea):** Light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ, *E*-isomer (***E*-3ea**): 8.29–8.25 (m, 2H), 8.08 (d, *J* = 12.8 Hz, 1 H), 7.80–7.25 (m, 7H), 6.63 (d, *J* = 12.8 Hz, 1H). *Z*-isomer (***Z*-3ea**): 5.91 (d, *J* = 7.2 Hz, 1H), other peaks were overlapped with those of the other isomers. Markovnikov adduct (1-phenylvinyl 4-(trifluoromethyl)benzoate, **4ea**): 5.61 (d, *J* = 2.6 Hz, 1H), 5.19 (d, *J* = 2.6 Hz, 1H), other peaks were overlapped with those of the other isomers. HRMS: Calculated for $C_{16}H_{11}F_3O_2$ (M): 292.0711; found: 292.0718.

Styryl 2,4,6-trimethylbenzoate (*E*-3fa, ***Z*-3fa** and **4fa):** Orange oil. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ, *E*-isomer (***E*-3fa**): 8.11 (d, *J* = 12.4 Hz, 1H), 7.57–7.19 (m, 5H), 6.90 (s, 2H), 6.48 (d, *J* = 12.4 Hz, 1H), 2.36 (s, 6H), 2.31 (s, 3H). *Z*-isomer (***Z*-3fa**): 6.91 (s, 2H), 5.81 (d, *J* = 7.2 Hz, 1H), 2.34 (s, 6H), 2.32 (s, 3H), other peaks were overlapped with those of the other isomers. Markovnikov adduct (1-phenylvinyl 2,4,6-trimethylbenzoate, **4fa**): 5.56 (d, *J* = 1.6 Hz, 1H), 5.19 (d, *J* = 1.6 Hz, 1H), other peaks were overlapped with those of the other isomers. HRMS: Calculated for $C_{18}H_{19}O_2$ (M+H): 267.1385; found: 267.1383.

Styryl thiophene-2-carboxylate (*E*-3ga, ***Z*-3ga** and **4ga):** Light brown oil. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ, *E*-isomer (***E*-3ga**): 8.02 (d, *J* = 12.8 Hz, 1H), 7.97–7.14 (m, 8H), 6.56 (d, *J* = 12.8 Hz, 1H). *Z*-isomer (***Z*-3ga**): 5.82 (d, *J* = 7.2 Hz, 1H), other peaks were overlapped with those of the other isomers. Markovnikov adduct (1-phenylvinyl thiophene-2-carboxylate, **4ga**): 5.58 (d, *J* = 2.8 Hz, 1H), 5.18 (d, *J* = 2.8 Hz, 1H), other peaks were overlapped with those of the other isomers. HRMS: Calculated for

$C_{13}H_{10}O_2S$ (M): 230.0402; found: 230.0403.

Styryl furan-3-carboxylate (*E*-3ha, *Z*-**3ha** and **4ha):** Light brown oil. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ, *E*-isomer (*E*-**3ha**): 8.17–8.14 (m, 1H), 8.01 (d, *J* = 12.6 Hz, 1H), 7.62–7.22 (m, 6H), 6.83 (m, 1H), 6.51 (d, *J* = 12.6 Hz, 1H). *Z*-isomer (*Z*-**3ha**): 5.81 (d, *J* = 7.2 Hz, 1H), other peaks were overlapped with those of the other isomers. Markovnikov adduct (1-phenylvinyl furan-3-carboxylate, **4ha**): 5.56 (d, *J* = 2.4 Hz, 1H), 5.14 (d, *J* = 2.4 Hz, 1H), other peaks were overlapped with those of the other isomers. HRMS: Calculated for $C_{13}H_{10}O_3$ (M): 214.0630; found: 214.0635.

Styryl octanoate (*E*-3ia, *Z*-**3ia** and **4ia):** Orange oil. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ, *E*-isomer (*E*-**3ia**): 7.87 (d, *J* = 12.6 Hz, 1H), 7.59–7.20 (m, 5H), 6.38 (d, *J* = 12.6 Hz, 1H), 2.54–2.41 (m, 2H), 1.77–1.65 (m, 2H), 1.35–1.29 (m, 8H), 0.90–0.87 (m, 3H). *Z*-isomer (*Z*-**3ia**): 5.69 (d, *J* = 7.2 Hz, 1H), other peaks were overlapped with those of the other isomers. Markovnikov adduct (1-phenylvinyl octanoate, **4ia**): 5.46 (d, *J* = 2.0 Hz, 1H), 5.01 (d, *J* = 2.0 Hz, 1H), other peaks were overlapped with those of the other isomers. HRMS: Calculated for $C_{16}H_{22}O_2$ (M): 246.1620; found: 246.1626.

4-Methoxystyryl benzoate (*E*-3ac, *Z*-**3ac** and **4ac):** Brown oil. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ, *E*-isomer (*E*-**3ac**): 8.20–8.13 (m, 2H), 7.99 (d, *J* = 12.6 Hz, 1H), 7.65–7.31 (m, 5H), 6.95–6.85 (m, 2H), 6.55 (d, *J* = 12.6 Hz, 1H), 3.81 (s, 3H). *Z*-isomer (*Z*-**3ac**): 5.80 (d, *J* = 6.8 Hz, 1H), 3.83 (s, 3H), other peaks were overlapped with those of the other isomers. Markovnikov adduct (1-(4-methoxyphenyl)vinyl benzoate, **4ac**): 5.46 (d, *J* = 2.2 Hz, 1H), 5.05 (d, *J* = 2.2 Hz, 1H), 3.79 (s, 3H), other peaks were

overlapped with those of the other isomers. HRMS: Calculated for $C_{16}H_{14}O_3$ (M): 254.0943; found:253.0940.

2-(Thiophen-3-yl)vinyl benzoate (*E*-3ad, ***Z*-3ad** and **4ad):** Dark brown oil. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ, *E*-isomer (***E*-3ad**): 8.20–8.16 (m, 2H), 8.01 (dd, *J* = 12.8, 1.6 Hz, 1H), 7.64–7.16 (m, 6H), 6.60 (d, *J* = 12.8 Hz, 1H). *Z*-isomer (***Z*-3ad**): 5.94 (d, *J* = 7.6 Hz, 1H), other peaks were overlapped with those of the other isomers. Markovnikov adduct (1-(thiophen-3-yl)vinyl benzoate, **4ad**): 5.47 (m, 1H), 5.11 (m, 1H), other peaks were overlapped with those of the other isomers. HRMS: Calculated for $C_{13}H_{10}O_2S$ (M): 230.0402; found: 230.0400.

1-(Pyridin-2-yl)vinyl benzoate (*E*-3ae and **4ae):** Dark brown oil. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ, Markovnikov adduct (**4ae**): 8.62–8.59 (m, 1H), 8.23–8.11 (m, 2H), 7.69–7.14 (m, 6H), 6.21 (d, *J* = 1.6 Hz, 1H), 5.36 (d, *J* = 1.6 Hz, 1H). *E*-isomer ((*E*)-2-(pyridin-2-yl)vinyl benzoate, ***E*-3ae**): 8.52 (d, *J* = 12.8 Hz, 1H), 6.66 (d, *J* = 12.8 Hz, 1H), other peaks were overlapped with those of the other isomers. HRMS: Calculated for $C_{14}H_{12}NO_2$ (M+H): 226.0868; found: 226.0864.

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Chapter 6

Selective addition of carboxylic acids to alkynes in the presence of recyclable ruthenium catalysts prepared through phosphine-modification of ruthenium(IV) species supported on ceria

6.1 Introduction

The development of highly selective catalytic reactions with high atom efficiencies is quite important, since such processes should give the desired products without by-products or wastes [1]. To achieve such goals, transition-metal complexes have been widely applied as homogeneous catalysts, mainly because fine-tuning of their active sites by ligands or additives can induce the excellent activities and selectivities. In this context, ruthenium complex catalysts together with suitable phosphine ligands have been used to accomplish the regio- and stereo-selective addition of carboxylic acid to alkynes [2–10], which is the most atom-economical route for the synthesis of vinyl esters [11].

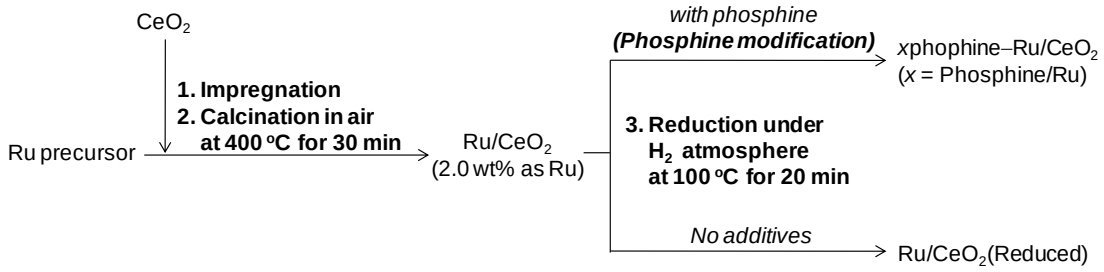
The use of solid catalysts, particularly oxide-supported metal catalysts, is quite attractive because of their simple preparation, high stability and facile reusability, as well as minimal contamination of the products by metallic species [12]. As described in the previous chapters, Ru/CeO_2 is quite effective catalysts for various synthetic reactions including the addition of carboxylic acids to terminal alkynes [13,14].

Furthermore, the heating of the Ru/CeO_2 catalysts in a hydrogen atmosphere in the presence of a small amount of phosphines (phosphine-modification) was found to greatly improve the activities of the resulting Ru catalysts for the arylation [13c] and alkylation [13d] of aromatic C–H bonds. On the basis of these results, modifications of Ru/CeO_2 by suitable phosphines are expected to generate highly active Ru catalysts for the regio- and stereo-selective syntheses of vinyl esters via the addition of carboxylic acids to alkynes.

In this chapter, a simple method for the preparation of active Ru catalysts that are applicable to the selective addition of carboxylic acids to terminal alkyne is described. The conditions of the pretreatment of Ru/CeO_2 catalysts greatly affected their catalytic behavior. The states of catalytically active species are discussed on the basis of spectroscopic characterization.

6.2 Results and discussion

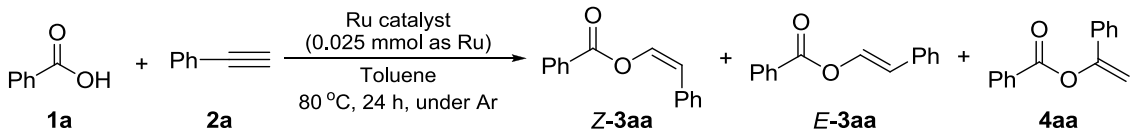
The methods for the preparation of supported Ru catalysts are summarized in Scheme 1. The CeO_2-supported Ru catalysts (Ru/CeO_2) were prepared by the impregnation of a solution of a Ru precursor, such as $RuCl_3 \cdot nH_2O$ or $Ru(acac)_3$, on CeO_2 followed by calcination in air at 400 °C for 30 min. The Ru/CeO_2 catalyst was then heated at 100 ^oC for 20 min under a hydrogen atmosphere (1 atm) without any solvent in the presence of phosphines to give *x*phosphine–Ru/CeO_2 (*phosphine modification)*, where *x* shows the molar ratio of phosphine to ruthenium. In contrast, the Ru/CeO_2 catalyst that was reduced under similar conditions in the absence of any additives was designated as Ru/CeO_2(Reduced).



Scheme 1. Method for the preparation of supported Ru catalysts.

1,4-Bis(diphenylphosphino)butane-modified Ru/CeO_2 catalyst (dppb-Ru/CeO_2) showed excellent activity for the selective addition of benzoic acid (**1a**) to ethynylbenzene (**2a**) to afford the corresponding vinyl ester **3aa** quantitatively, with high selectivity for the (*Z*)-isomer (Table 1, entry 1). On the other hand, the reaction catalyzed by unmodified Ru/CeO_2 without any external additives mainly afforded the (*E*)-isomer of **3aa** (entry 2). Note that Ru/CeO_2-catalyzed reaction at 130 ^oC gave the product *E*-**3aa** in a high yield as described in chapter 5 [14]. Ruthenium complexes with the dppb ligand were reported to act as effective homogeneous catalysts to afford the (*Z*)-isomer of vinyl esters with excellent selectivities [7]. The addition of dppb to the unmodified Ru/CeO_2-catalyzed system produced the (*Z*)-isomer of **3aa** with a high selectivity, whereas the total yield of vinyl esters was very low (entry 3). The pre-reduction of Ru/CeO_2 with molecular hydrogen did not have a positive effect (entry 4) and the reaction of **1a** with **2a** carried out under a hydrogen atmosphere resulted in a moderate total yield of **3aa** (entry 5). These results indicated that the reductive treatment of Ru/CeO_2 catalysts *in the presence of phosphine* is essential for generating Ru species with high catalytic activity and selectivity.

Table 1. Effect of pretreatment of Ru/CeO_2 catalysts.[a]

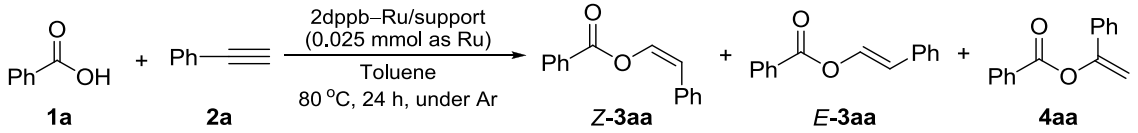


Entry	Ru catalyst	Total yield (%)[b]	Selectivity (%)[c] (*Z*-**3aa** : *E*-**3aa**: **4aa**)
1	2dppb–Ru/CeO_2	99	90 : 10 : 0
2	Ru/CeO_2	24	13 : 83 : 4
3	Ru/CeO_2 + dppb	18	89 : 11 : 0
4	Ru/CeO_2 (Reduced) + dppb	18	90 : 10 : 0
5[d]	Ru/CeO_2 + dppb	50	90 : 10 : 0

[a] *Reaction conditions*: **1a** (1.0 mmol), **2a** (1.3 mmol), toluene (1.0 mL), Ru/CeO_2 (prepared from $RuCl_3 \cdot nH_2O$, 0.025 mmol as Ru), dppb (0.050 mmol), at 80 °C for 24 h under Ar. [b] Total yield of **3aa** and **4aa** based on **1a**, determined by GLC. [c] Molar ratio of isomers determined by GLC. [d] Reaction under H_2 (1 atm).

Effect of Ru precursors and support for the activities of dppb-modified Ru catalysts was examined (Table 2, entries 1–5). The solid Ru/CeO_2 catalyst prepared using $Ru(acac)_3$ showed the highest selectivity and the reaction was complete in the shortest time (8 h, entry 5). The Ru/ZrO_2 catalyst modified by dppb also showed the catalytic activity for the selective addition (entry 6). In contrast, the dppb-modified Ru catalysts supported on SiO_2, Al_2O_3, TiO_2 or MgO did not show any activity (entries 7–10). Such a marked effect of the support has been observed in our previous studies on C–C bond-forming reactions [13] as well as the addition of carboxylic acids to alkynes by unmodified catalysts [14]. As discussed in the previous chapters, highly-dispersed Ru(IV)-oxo species is selectively formed on the surface of ceria and zirconia, which would be a good precursor of the catalytically active Ru species. In contrast, Ru species formed on the surface of the other supports had a microstructure similar to that of crystalline RuO_2, which could not be transformed into the active catalysts.

Table 2. Effect of Ru precursor and support.[a]



Entry	Support	Ru precursor	Total yield (%)[b]	Selectivity (%)[c] ***Z*-3aa** : ***E*-3aa** : **4aa**
1	CeO_2	$RuCl_3 \cdot nH_2O$	99	90 : 10 : 0
2	CeO_2	$[RuCl_2(p\text{-cymene})]_2$	64	97 : 3 : 0
3	CeO_2	$[RuCl_2(CO)_3]_2$	99	91 : 9 : 0
4	CeO_2	$Ru_3(CO)_{12}$	83	91 : 9 : 0
5[d]	CeO_2	$Ru(acac)_3$	99	98 : 2 : 0
6	ZrO_2	$Ru(acac)_3$	71	98 : 2 : 0
7	SiO_2	$Ru(acac)_3$	0	-
8	Al_2O_3	$Ru(acac)_3$	trace	-
9	TiO_2	$Ru(acac)_3$	0	-
10	MgO	$Ru(acac)_3$	0	-

[a] *Reaction conditions*: **1a** (1.0 mmol), **2a** (1.3 mmol), toluene (1.0 mL), Ru/support (prepared from $RuCl_3 \cdot nH_2O$, 0.025 mmol as Ru, dppb 0.050 mmol), at 80 °C for 24 h under Ar.
[b] Total yield of **3aa** and **4aa** based on **1a**, determined by GLC. [c] Molar ratio of isomers determined by GLC. [d] Reaction for 8 h.

To examine the state of ruthenium species on Ru/CeO_2 before and after modification with dppb, Ru K-edge X-ray absorption near edge structure (XANES) spectra were recorded, and the results are shown in Figure 1 together with the spectra of RuO_2 and Ru metal. The XANES spectrum of unmodified Ru/CeO_2 showed a characteristic pre-edge peak at around 22110 eV, which is assignable to Ru(IV) species with a distorted coordination structure bearing a Ru=O bond [13e,15]. After dppb-treatment, the pre-edge peak disappeared, and the absorption-edge of the catalyst shifted to a lower energy but did not coincide with that of Ru metal. This result indicates that the Ru(IV) species are reduced to low-valent Ru species, probably Ru(II) species, with a loss of the Ru=O structure.

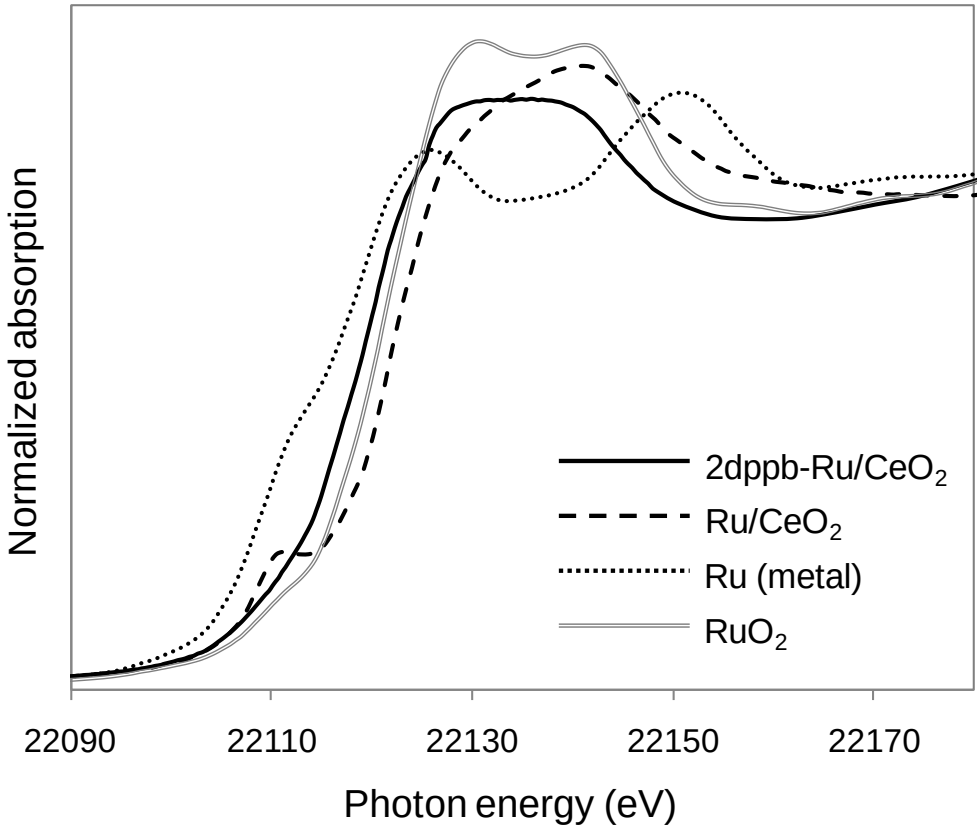
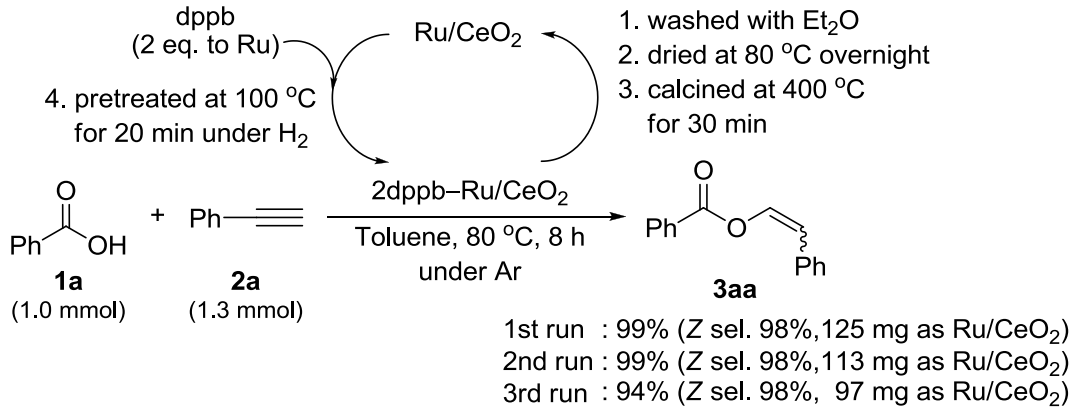


Figure 1. Ru K-edge XANES spectra of the catalysts.

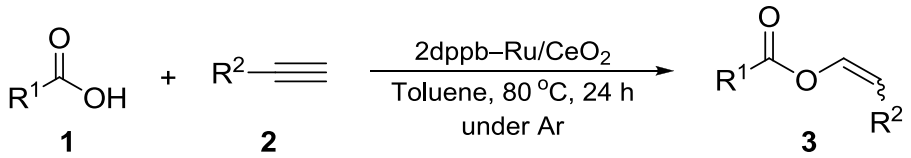
One major advantage of solid catalysts is their high recyclability. Scheme 2 shows an outline of the successful regeneration procedure and the results of catalytic reactions with the recycled catalysts. After the reaction, the dppb-modified Ru/CeO_2 catalyst was washed with diethyl ether (10 mL, 3 times), dried in air at 80 ^oC, and then calcined in air at 400 ^oC to be recovered as Ru/CeO_2. The thus-obtained solid was re-modified with dppb under a hydrogen atmosphere to give the regenerated dppb–Ru/CeO_2 for the next catalytic run. Whereas a slightly decreased amount of the recycled catalyst was used, *Z*-**3aa** was successfully obtained in excellent yields and selectivities in the 2nd and 3rd runs. On the other hand, the reaction using recovered Ru catalysts without calcination and further dppb-modification resulted in low yields of **3aa**, probably because of the deactivation of Ru catalys.

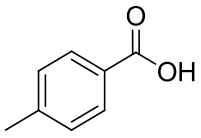
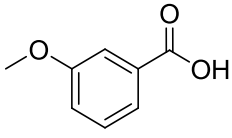


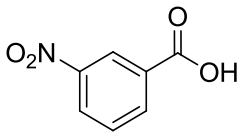
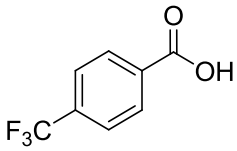
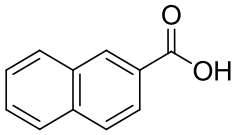
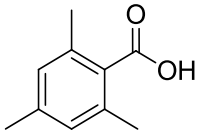
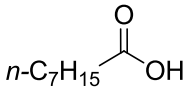
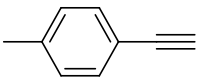
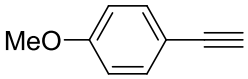
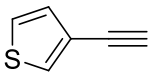
Scheme 2. Recycling of the dppb-modified Ru/CeO_2 catalyst.

The results of the reactions of various carboxylic acids with terminal alkynes by the dppb-modified Ru/CeO_2 catalyst are summarized in Table 3. The reaction with aromatic carboxylic acids bearing an electron-donating or -withdrawing substituent on the phenyl ring as well as 2-naphthoic acid proceeded smoothly to afford the corresponding vinyl esters in high yields with excellent (*Z*)-isomer selectivities. The reaction with an aliphatic carboxylic acid (**1h**) also gave the desired (*Z*)-adduct with a high selectively. The reactions of **1a** with aromatic and heteroaromatic terminal alkynes also produced the (*Z*)-isomer of the adducts with excellent selectivities. Note that formation of the Markovnikov adducts (**4**) was not observed at all in the reaction shown in Table 3.

Table 3. *Z*-Selective addition of carboxylic acids to terminal alkynes by dppb–Ru/CeO_2 catalyst.[a]



Entry	**1**	**2**	Product	Yield of **3** (%) [b]	Sel. (*Z* : *E*) [c]
1	 **1b**	**2a**	**3ba**	88	98 : 2
2	 **1c**	**2a**	**3ca**	95	100 : 0

3	 **1d**	**2a**	**3da**	76	98: 2
4	 **1e**	**2a**	**3ea**	61	98 : 2
5	 **1f**	**2a**	**3fa**	90	93 : 7
6	 **1g**	**2a**	**3ga**	42	85 : 15
7	 **1h**	**2a**	**3ha**	48	94 : 6
8	**1a**	 **2b**	**3ab**	65	100 : 0
9	**1a**	 **2c**	**3ac**	66	98 : 2
10	**1a**	 **2d**	**3ad**	94	100 : 0

[a] *Reaction conditions*: **1** (1.0 mmol), **2** (1.3 mmol), toluene (1.0 mL), dppb–Ru/CeO_2 (0.025 mmol, prepared from $Ru(acac)_3$, dppb 0.050 mmol), at 80 °C for 24 h under Ar. [b] Isolated yield. [c] Molar ratio of isomers determined by ^1H NMR.

The amount of ruthenium species leached from the solid Ru catalysts into the liquid phase after the reactions of **1a** with **2a** under the condition shown in Table 1 were examined by inductively coupled plasma atomic emission spectrometry (ICP-AES). From the 2dppb–Ru/CeO_2 catalyst, 0.54 μmol of Ru species were found to be leached into toluene solution after it was allowed to cool to room temperature, which corresponds to 2.2% of ruthenium species in the fresh 2dppb–Ru/CeO_2 catalyst. the amount of ruthenium species leached from the zirconia-supported catalyst was below the detection limit in the ICP-AES measurement. To investigate the contribution of the soluble ruthenium species generated from the 2dppb–Ru/CeO_2 catalyst, the effects of the removal of the solid catalysts by hot filtration through a PTFE filter (pore size 0.45 μm) were examined [16,17]. Figure 2 shows the time-course of the reactions with or without hot filtration. Removal of the solid catalyst after the reaction for 1 h did not stop further progress of the reaction. ICP-AES showed that the solution after hot filtration contained 1.3% of Ru species in the fresh catalyst. The results of the present hot filtration tests are very different than those observed in the C–C bond-forming reactions by PPh_3-modified Ru/CeO_2 catalyst, where removal of the solid catalysts stopped further progress of the reactions [13c]. These suggest that the contribution of dissolved ruthenium species depends on the type of the reaction, and that in the present catalytic reaction, Ru/CeO_2 acted as an excellent source for extremely active, soluble ruthenium species.

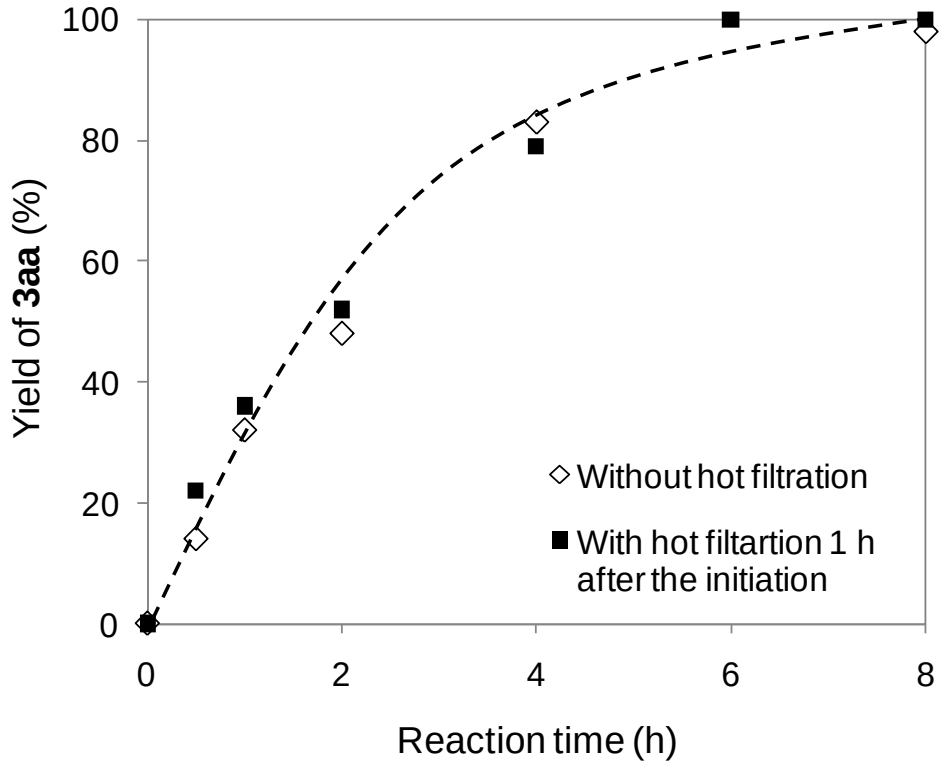
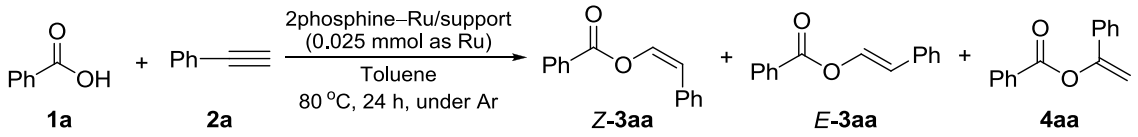


Figure 2. Effects of catalyst removal by hot filtration on the reaction of **1a** with **2a** at 80 °C catalyzed by 2dppb–Ru/CeO_2 catalysts.

Next, we focused our efforts on the selective production of Markovnikov-adducts **4** by the use of the Ru/CeO_2 catalysts. Effects of the class of phosphines for the reaction of **1a** with **2a** at 80 °C in toluene were examined (Table 4). Tributylphosphine-, 1,1-bis(diphenylphosphino)methane- (dppm-) or trioctylphosphine-modified Ru/CeO_2 catalyst have been found to give **4aa** as a major product (entries 2, 8 and 9). The modification by other phosphines, PPh_3, *rac*-BINAP, and 1,2-bis(diphenylphophino)ethane (dppe) completely suppressed the activity under the present conditions (entries 1, 3 and 7).

Table 4. Effect of phosphines for modification of Ru/CeO_2.[a]

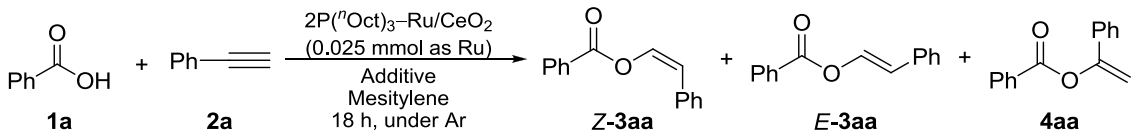


Entry	Phosphine	Total yield (%)[b]	Selectivity (%)[c] *Z*-**3aa** : *E*-**3aa** : **4aa**
1	PPh_3	trace	—
2	dppm	68	26 : 8 : 66
3	dppe	0	—
4	dppp	7	86 : 14 : 0
5[d]	dppb	99	98 : 2 : 0
6	dpppe	7	100 : 0 : 0
7	*rac*-BINAP	trace	—
8	$P(^nBu)_3$	57	11 : 7 : 82
9	$P(^nOct)_3$	71	11: 21 : 68

[a] *Reaction conditions*: **1a** (1.0 mmol), **2a** (1.3 mmol), toluene (1.0 mL), Ru catalyst (0.025 mmol as Ru, prepared from $Ru(acac)_3$, phosphine 0.050 mmol), at 80 °C for 24 h under Ar. [b] Total yield of **3aa** and **4aa** based on **1a**, determined by GLC. [c] Molar ratio of isomers determined by GLC. [d] Reaction time, 8 h.

Then, further optimization of the reaction conditions for the selective synthesis of Markovnikov-adducts was examined (Table 5). When the reaction was carried out at 120 ^{o}C, **3aa** and **4aa** was obtained in the highest total yield, whereas the selectivity of **4aa** was moderate (entries 1–3). However, the addition of a small amount of ammonium chloride was found to induce the Markovnikov-selective addition, and the addition of 0.10 mmol (4 eq. to Ru) of NH_4Cl was found to be suitable in terms of both the yield of vinyl esters and the selectivity for **4aa** (entry 9). The addition of a larger or smaller amount of NH_4Cl decreased the total yield and the selectivity for **4aa** (entries 10–12).

Table 5. Effect of reaction temperature and additives on the reaction catalyzed by P(^{n}Oct)$_3$-modified Ru/CeO_2.[a]

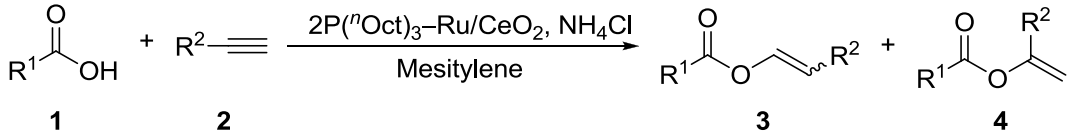


Entry	Additive (mmol)	Temperature (°C)	Total yield (%)[b]	Selectivity (%)[c] *Z*-**3aa** : *E*-**3aa** : **4aa**
1[d]	None	80	71	11 : 21 : 68
2[d]	None	120	99	26 : 27 : 47
3[d]	None	140	81	31 : 7 : 62
4	KI (0.10)	120	92	28 : 33 : 39
5	KBr (0.10)	120	99	26 : 15 : 59
6	KCl (0.10)	120	99	24 : 11 : 65
7	LiCl (0.10)	120	92	28 : 50 : 22
8	NaCl (0.10)	120	83	19 : 6 : 75
9[e]	NH_4Cl (0.10)	120	99	15 : 8 : 77
10	NH_4Cl (0.050)	120	69	29 : 28 : 43
11	NH_4Cl (0.20)	120	82	15 : 21 : 64
12	NH_4Cl (0.40)	120	88	39 : 20 : 41

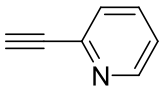
[a] *Reaction conditions*: **1a** (1.0 mmol), **2a** (1.3 mmol), mesitylene (1.0 mL), Ru catalyst (0.025 mmol as Ru, prepared from Ru(acac)$_3$, P(^{n}Oct)$_3$, 0.050 mmol), for 18 h under Ar. [b] Total yield of **3aa** and **4aa** based on **1a**, determined by GLC. [c] Molar ratio of isomers determined by GLC. [d] Reaction time, 24 h. [e] Reaction time, 6 h.

Although there is still room for further optimization of the reaction conditions, various Markovnikov adducts **4** were obtained in good to high selectivities under the present conditions (Table 6): for example, the reaction of **1d** with **2a** in the presence of 2P(^{n}Oct)$_3$–Ru/CeO_2 catalyst together with NH_4Cl in mesitylene at 120 ^{o}C produced **4da** with 91% selectivity (entry 4).

Table 6. Addition of various carboxylic acids to terminal alkynes by P(^{n}Oct)$_3$–Ru/CeO_2 catalyst.[a]



1 **2** **3** **4**

Entry	**1**	**2**	Products	Total yield (%)[b]	Selectivity (*Z*-**3** : *E*-**3** : **4**)[c]
1[d]	**1a**	**2a**	**3aa** + **4aa**	99	15 : 8 : 77
2	**1a**	**2b**	**3ab** + **4ab**	81	9 : 6 : 85
3	**1d**	**2a**	**3da** + **4da**	68	5 : 4 : 91
4	**1c**	**2a**	**3ca** + **4ca**	80	18 : 32 : 50
5	**1a**	 **2e**	**3ae** + **4ae**	37	0 : 9 : 91

[a] *Reaction conditions*: **1** (1.0 mmol), **2** (1.3 mmol), mesitylene (1.0 mL), P(^{n}Oct)$_3$–Ru/CeO_2 (0.025 mmol as Ru, prepared from Ru(acac)$_3$, P(^{n}Oct)$_3$ 0.050 mmol), NH_4Cl (0.10 mmol), at 120 °C for 18 h under Ar. [b] Isolated yield.
[c] Molar ratio of isomers determined by ^{1}H NMR. [d] Reaction for 6 h.

6.3 Conclusions

In this chapter, the simple modification of Ru/CeO_2, i.e., reduction under a hydrogen atmosphere in the presence of suitable phosphines, was found to generate Ru catalysts that are effective for regio- and stereo-selective addition of carboxylic acids to alkynes. The 2dppb–Ru/CeO_2 catalyst gave (*Z*)-isomers of anti-Markovnikov adducts with excellent selectivities. On the other hand, the $P(^nOct)_3$-modified Ru/CeO_2 catalysts gave the Markovnikov adducts as major products. These catalysts could be used for a variety of carboxylic acids and terminal alkynes and could be recycled without a significant loss of activity. Hot filtration tests and the ICP-AES analyses suggest that a very small amount of ruthenium species acted as catalysts in the solution phase. The catalysts demonstrated in the present study are attractive and advantageous from synthetic, industrial, and environmental points of view.

6.4 Experimental

6.4.1 Materials and methods

All manipulations were performed under an argon atmosphere using standard Schlenk techniques. Dehydrated methanol, tetrahydrofuran (THF), and toluene were obtained from Wako and were used as received. Other organic and inorganic reagents were commercially available and used without further purification. Cerium oxide was prepared by the treatment of a solution of cerium(III) nitrate hexahydrate (Wako, 12.6 g, 29 mmol) in 400 mL of deionized water with 40 mL of 3 M KOH aqueous solution with stirring for 2 h at room temperature. The resulting precipitate was collected by centrifugation, and then air-dried overnight at 80 °C. The product was heated in a box furnace at a rate of 10 °C min^{-1} and maintained at 400 °C for 30 min to afford ceria in an excellent ceramic yield. Zirconium oxide and magnesium oxide were prepared by the same method using zirconium oxynitrate and magnesium nitrate hexahydrate, respectively. Titanium oxide (JRC-TIO-4) and γ-alumina (JRC-ALO-8) were obtained from the Catalysis Society of Japan. Silica (CAB-O-SIL) was obtained from Cabot and used as received.

6.4.2 Characterizations

NMR spectra were recorded on a JEOL JNM-EX-400 (FT, 400 MHz (^{1}H)) instrument. ^{1}H and $^{13}C\{^1H\}$ chemical shifts (δ) were referenced to $SiMe_4$. High-resolution mass spectra (FAB) were recorded on a JEOL SX102A spectrometer with *m*-nitrobenzyl alcohol as a matrix. Ru K-edge X-ray absorption fine structure (XAFS) measurements were performed at the BL01B1 beam line at SPring-8 operated at 8 GeV using a Si(311) two-crystal monochromator at room temperature. X-ray

absorption near edge structure (XANES) spectra were analyzed using the Rigaku REX 2000 version 2.5 program.

The leaching of ruthenium species from the catalysts during the reaction was investigated by inductively coupled plasma atomic emission spectroscopy (ICP-AES) using a Shimadzu ICPS-1000III analyzer. The products of catalytic runs were analyzed by GC–MS (Shimadzu GC–MS Parvum 2; Zebron ZB-1 capillary column, i.d. 0.25 mm, length 30 m, at 50–250 °C) and gas–liquid chromatography (GL Sciences GC353; Inertcap 17 capillary column, i.d. 0.25 mm, length 30 m at 50–250 °C).

6.4.3 Preparation of supported Ru catalysts

Supported catalysts were prepared by the impregnation method using various supports and ruthenium complexes. A typical procedure is as follows: 1.0 g of metal oxide was added to a solution of 79 mg (0.20 mmol, 20 mg as Ru) of $Ru(acac)_3$ (Aldrich) in 10 mL of THF under air at room temperature. For $Ru_3(CO)_{12}$ (Strem Chemicals) and $[RuCl_2(CO)_3]_2$ (Strem Chemicals), THF was used as a solvent, while $RuCl_3 \bullet nH_2O$ (Tanaka Kikinzoku Kogyo) and $[RuCl_2(p\text{-cymene})]_2$ (Strem Chemicals) were impregnated from their methanol solutions. After impregnation and drying overnight in air at 80 °C, the resulting powder was calcined in air at 400 °C for 30 min to afford the Ru(2.0 wt%)/support catalyst.

6.4.4 Modification of the catalysts by phosphines

Modification of the Ru/support catalysts by dppb was performed as follows: 125 mg (0.025 mmol as Ru) of Ru/support and dppb (22 mg, 0.050 mmol) were heated at 100 °C for 20 min under a hydrogen atmosphere (1 atm) without any solvent. The

resulting catalysts were designated as *x*dppb–Ru/support (*x* = molar ratio of dppb to Ru). P(^{n}Oct)$_3$-modified Ru/support catalysts were prepared by the same method using 19 mg (0.050 mmol) of P(^{n}Oct)$_3$ instead of dppb. These phosphine-modified Ru/CeO_2 were used for the catalytic reaction without exposing to open air.

6.4.5 General procedure for the addition of carboxylic acids to terminal alkynes

All of the reactions were performed by the use of hot stirrers equipped with cooling blocks for refluxing the solution. A typical reaction procedure is as follows: A mixture of carboxylic acid (1.0 mmol) and terminal alkyne (1.3 mmol) in toluene (1.0 mL) was placed in a 20 mL glass Schlenk tube with a balloon under an Ar atmosphere together with the phosiphine-modified Ru(2.0 wt%)/CeO_2 catalyst (0.025 mmol as Ru, 125 mg as Ru/CeO_2). The reaction mixture was stirred at 80 °C for 24 h, and then cooled rapidly in an ice bath. After the reaction, the solid catalyst was removed by passing the mixture through a 0.45 μm PTFE filter (Millipore Millex LH), and the filtrate was concentrated under reduced pressure. The products were isolated by column chromatography (silica gel, 4:1; hexane/EtOAc, v/v), identified by GC–MS, ^{1}H and ^{13}C NMR, HRMS, and quantified by GLC analyses using biphenyl as an internal standard.

6.4.6 Recovery of the 2dppb–Ru/CeO_2 catalyst

After the reaction, the solid was separated from the reaction mixture by centrifugation and washed three times with 10 mL of diethyl ether. The resulting solid was dried overnight at 80 °C and calcined in air at 400 °C for 30 min to recover Ru/CeO_2. Modification of Ru by 2 equivalents of dppb was then performed through the aforementioned procedure to give the 2dppb–Ru/CeO_2 catalyst for reuse.

6.4.7 Hot filtration test

A 20 mL Schlenk tube was charged with benzoic acid (**1a**, 2.0 mmol), ethynylbenzene (**2a**, 2.6 mmol), toluene (2.0 mL), and the 2dppb–Ru(2.0 wt%)/CeO_2 catalyst (0.050 mmol as Ru) together with an internal standard (biphenyl, *ca*. 46 mg) under an argon atmosphere. After the reaction was allowed to proceed for 1 h at 80 °C, the mixture was filtered through a 0.45 μm syringe filter (Millipore Millex LH) into another preheated Schlenk tube. The filtrate was stirred at 80 °C, and the conversion and yields of the product after filtration were monitored by GC and GC–MS analyses.

6.4.8 Characterization Data of the Products

(*Z*)-Styryl 3-methoxybenzoate (*Z*-**3ca**): Orange oil. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) *δ*, 7.74 (m, 1H), 7.65 (m, 3H), 7.53 (d, J = 7.1 Hz, 1H), 7.37 (m, 3H), 7.25 (m, 1H), 7.13 (m, 1H), 5.83 (d, *J* = 7.1 Hz, 1H), 3.82 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) *δ*, 163.1, 159.6, 134.1, 134.0, 130.1, 129.6, 129.1, 128.4, 127.3, 122.4, 120.4, 114.2, 112.5, 55.2. HRMS: Calculated for $C_{16}H_{15}O_3$ (M+H): 255.1021; found: 255.1027.

(*Z*)-Styryl 3-nitrobenzoate (*Z*-**3da**): Yellowish white solid. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) *δ*, 9.02 (m, 1H), 8.48 (m, 2H), 7.74 (t, *J* = 8.3 Hz, 1H), 7.65 (d, *J* = 7.8 Hz, 2H), 7.54 (d, *J* = 7.0 Hz, 1H), 7.44 (t, *J* = 8.3 Hz, 2H), 7.32 (m, 1H), 5.95 (d, *J* = 7.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) *δ*, 161.4, 147.0, 135.6, 133.7, 133.5, 130.8, 130.1, 129.2, 128.6, 128.1, 127.8, 125.1, 113.8. HRMS: Calculated for $C_{15}H_{11}NO_4$ (M): 269.0688; found: 269.0680.

(*Z*)-Styryl 4-(trifluoromethyl)benzoate (*Z*-**3ea**): Light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ, 8.25 (d, J = 7.8 Hz, 2H), 7.77 (d, J = 7.8 Hz, 2H), 7.62 (d, J = 7.8 Hz, 2H), 7.52 (d, J = 7.0 Hz, 1H), 7.39 (t, J = 7.8 Hz, 2H), 7.29 (m, 1H), 5.89 (d, J = 7.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ, 162.3, 135.1 (q, J = 33.1 Hz), 133.9, 133.8, 132.2 (m), 131.5, 130.5, 129.2, 128.5, 127.6, 125.8 (m), 113.4. HRMS: Calculated for $C_{16}H_{11}F_3O_2$ (M): 292.0711; found: 292.0717.

(*Z*)-Styryl 2-naphthoate (*Z*-**3fa**): Light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ, 8.75 (br s, 1H), 8.17 (dd, J = 1.5, 8.3 Hz, 1H), 8.01–7.91 (m, 3H), 7.73 (d, J = 7.3 Hz, 2H), 7.66-7.57 (m, 3H), 7.43 (t, J = 7.8 Hz, 2H), 7.31 (t, J = 7.3 Hz, 1H), 5.91 (d, J = 6.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ, 163.6, 135.9, 134.3, 134.2, 132.5, 132.2, 129.5, 129.3, 128.8, 128.6, 128.5, 127.9, 127.4, 127.0, 126.1, 125.2, 112.7. HRMS: Calculated for $C_{19}H_{15}O_2$ (M+H): 275.1072; found: 275.1064.

(*Z*)-Styryl octanoate (*Z*-**3ha**): Orange oil. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ, 7.58 (d, J = 7.3 Hz, 2H), 7.36–7.22 (m, 4H), 5.69 (d, J = 7.3 Hz, 1H), 2.52 (t, J = 7.3 Hz, 2H), 1.73 (m, 2H), 1.40–1.28 (m, 8H), 0.88 (t, J = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ, 170.3, 134.1, 133.9, 129.1, 128.4, 127.2, 111.7, 34.2, 21.6, 29.0, 28.9, 24.7, 22.6, 14.0. HRMS: Calculated for $C_{16}H_{23}O_2$ (M+H): 247.1698; found: 247.1685.

(*Z*)-2-(Thiophen-3-yl)vinyl benzoate (*Z*-**3ad**): Dark brown oil. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ, 8.26 (d, J = 7.3 Hz, 2H), 7.63 (m, 1H), 7.53–7.46 (m, 5H), 7.33 (dd, J = 2.9, 4.9 Hz, 1H), 5.94 (d, J = 7.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ, 163.4, 134.8, 133.7, 133.2, 130.0, 129.0, 128.7, 128.4, 125.4, 124.2, 107.2. HRMS: Calculated

for $C_{13}H_{10}O_2S$ (M): 230.0402; found: 230.0405.

1-Phenylvinyl 3-nitrobenzoate (a mixture of **4da,** *E*-**3da** and *Z*-**3da** (91 : 4 : 5)): Orange oil. For **4da**, ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ, 9.03 (m, 1H), 8.51 (m, 2H), 7.73 (t, J = 7.8 Hz, 1H), 7.52 (m, 2H), 7.38 (m, 3H), 5.63 (d, J = 2.5 Hz, 1H), 5.21 (d, J = 2.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ, 162.7, 153.0, 148.4, 135.7, 133.7, 131.2, 129.9, 129.3, 128.7, 128.0, 125.0, 124.9, 102.8.

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Chapter 7

Intermolecular coupling of alkynes with acrylates by recyclable oxide-supported ruthenium catalysts: Formation of distorted ruthenium(IV)-oxo species on ceria as a key precursor of active species

7.1 Introduction

Highly efficient organic transformations with solid catalysts [1], in particular inorganic oxide-supported catalysts, contribute to the realization of green sustainable chemistry [2,3]. In general, the states of supported metal species are critically affected by the supports, and a particular support may completely change the nature of the metal species, which could show unexpected features in catalytic reactions [4].

As shown in previous chapters, various efficient organic transformations, such as the arylation of aromatic C–H bonds, in the presence of Ru/CeO_2 and Ru/ZrO_2 catalysts have been developed [5–8]. These simple catalysts could be recycled several times without a significant loss of ruthenium species from the oxide support. Ruthenium catalysts supported on SiO_2, Al_2O_3, TiO_2 and MgO were totally ineffective for these reactions, which demonstrates the specific effects of the combination of Ru species and CeO_2 or ZrO_2.

On the other hand, substituted 1,3-dienes are important organic intermediates in modern industrial chemistry and materials science [9]. Various methods for their

preparation through the use of organometallic reagents have been proposed [10]. Above all, the intermolecular coupling of alkynes with alkenes is one of the most atom-efficient strategies and has been achieved with a series of transition-metal complex catalysts, including Ru [11], Rh [12], Pd [13], Co [14] and Ni [15]. However, these homogeneous complex catalysts are difficult to prepare, highly sensitive toward air and moisture, and they often require the use of toxic phosphines as ligands for efficient catalysis. To the best of our knowledge, there has been no example of the synthesis of substituted 1,3-dienes *via* the intermolecular coupling of alkynes with alkenes by simple, stable and recyclable solid catalysts. In this chapter, the intermolecular coupling of alkynes with acrylates by oxide-supported catalysts, Ru/CeO_2 and Ru/ZrO_2, in the presence of sodium formate is described. Furthermore, the coupling of two different alkenes was also realized through the use of these simple catalysts. The solid catalysts could be recycled several times without a significant loss of activity. A detailed characterization of the supported Ru catalysts suggests that the distorted Ru(IV)-oxo species is present in the ceria support which was transformed into low-valent Ru species at the initial stage of the reaction, leading to efficient catalytic reactions.

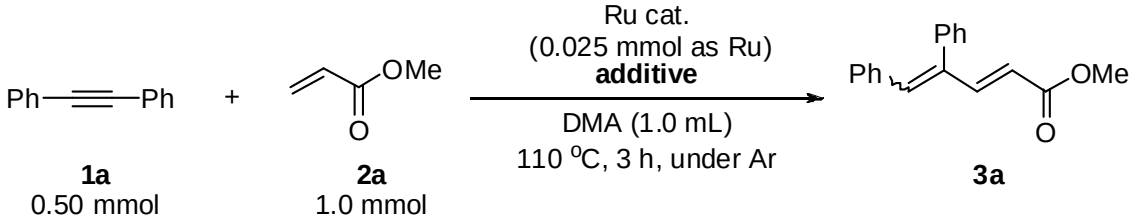
7.2 Results and discussion

Supported Ru catalysts were prepared by an impregnation method using $Ru(acac)_3$ as a Ru precursor, followed by calcination in air, and are designated as Ru/support-XXcal (where XX indicates the calcination temperature in Celsius).

The reaction of diphenylacetylene (**1a**) with methyl acrylate (**2a**) in the presence of Ru/CeO_2-400cal (125 mg, 0.025 mmol as Ru) together with a catalytic amount of sodium formate in *N*,*N*-dimethylacetamide (DMA) at 110 ^{o}C for 3 h gave 1,3-diene **3a** in a yield of 98% with a high *Z* selectivity at the γ,δ-position (Table 1, entry 1). No reaction occurred in the absence of sodium formate, even at a higher temperature (entries 2 and 3). The use of sodium acetate instead of sodium formate did not afford **3a** at all (entry 4). The treatment of Ru complexes by formate has been reported to produce Ru–H species [16, 17a], which were thought to play a key role in the present coupling reaction [17]. The addition of sodium borohydride, 2-propanol or isobutyryl chloride as hydride sources to the reaction mixture was ineffective, and the reaction under an hydrogen atmosphere resulted in a low yield of **3a** (entries 5–8). The addition of PPh_3 completely suppressed the reaction (entry 9), although ruthenium phosphine complexes have been reported to be effective precursors for homogeneous catalysts [11c,g].

Among other supported Ru catalysts examined, Ru/ZrO_2 showed high activity (entry 10). In contrast, no reaction took place with Ru catalysts supported on SiO_2, Al_2O_3, TiO_2 or MgO (entries 11–14). Note that air- and moisture-stable Ru complexes, $Ru(acac)_3$, $RuCl_3 \cdot nH_2O$ and $[RuCl_2(p\text{-cymene})]_2$, were not very effective under the present conditions (entries 15–17).

Table 1. Effects of additives and supports.



1a 0.50 mmol

2a 1.0 mmol

3a

Entry	Ru catalyst	Additive (mmol)	Yield (%)[a,b]
1	Ru/CeO_2-400cal	HCO_2Na (0.15)	98 (93:7)
2	Ru/CeO_2-400cal	-	0
3[c]	Ru/CeO_2-400cal	-	0
4	Ru/CeO_2-400cal	CH_3CO_2Na (0.15)	0
5	Ru/CeO_2-400cal	$NaBH_4$ (0.15)	8
6	Ru/CeO_2-400cal	2-PrOH (0.30)	0
7	Ru/CeO_2-400cal	Isobutyryl chloride (0.15)	0
8[d]	Ru/CeO_2-400cal	H_2 (1 atm)	11
9	Ru/CeO_2-400cal	HCO_2Na (0.15) PPh_3 (0.050)	trace
10	Ru/ZrO_2-400cal	HCO_2Na (0.15)	93 (95:5)
11	Ru/SiO_2-400cal	HCO_2Na (0.15)	0
12	Ru/Al_2O_3-400cal	HCO_2Na (0.15)	trace
13	Ru/TiO_2-400cal	HCO_2Na (0.15)	0
14	Ru/MgO-400cal	HCO_2Na (0.15)	trace
15	$Ru(acac)_3$	HCO_2Na (0.15)	trace
16	$RuCl_3 \cdot nH_2O$	HCO_2Na (0.15)	21
17	$[RuCl_2(p\text{-cymene})]_2$	HCO_2Na (0.15)	15

[a] Determined by GLC. [b] γ,δ-*Z*/*E*-Selectivities in parentheses. [c] Reaction at 170 °C.
[d] Reaction under H_2 (1 atm) atmosphere.

In previous chapters, although Ru/CeO_2- and Ru/ZrO_2-catalyzed organic synthetic reactions were described [5−8], the effects of the support have not been fully explained. Therefore, the states of Ru species on the supported catalysts before the catalytic runs were investigated by various method including detailed spectroscopic analyses.

The BET surface areas of supported Ru catalysts calcined at 400 ^oC were characterized by nitrogen gas adsorption. The results are summarized in Table 2. The surface areas of Ru/CeO_2 and Ru/ZrO_2 were 102 and 95 m^2g^{-1}, respectively. Although Ru/SiO_2, Ru/Al_2O_3 and Ru/MgO have higher surface areas, they were not effective catalysts for the present reactions.

Table 2. Characterization data of supported Ru catalysts by nitrogen gas adsorption.

Entry	Ru catalyst	Surface area (m^2g^{-1})
1	Ru/CeO_2-400cal	102
2	Ru/ZrO_2-400cal	95
3	Ru/SiO_2-400cal	269
4	Ru/Al_2O_3-400cal	142
5	Ru/MgO-400cal	148
6	Ru/TiO_2-400cal	49

XRD patterns of supported Ru catalysts calcined at 400 °C are shown in Figure 1. Although the peaks due to crystalline RuO_2 were observed for Ru catalysts supported on SiO_2 and Al_2O_3, they did not appear for Ru/CeO_2. This indicates that Ru species on CeO_2 are highly dispersed. Although peaks due to RuO_2 were not observed on MgO or TiO_2, these catalysts did not show any catalytic activities.

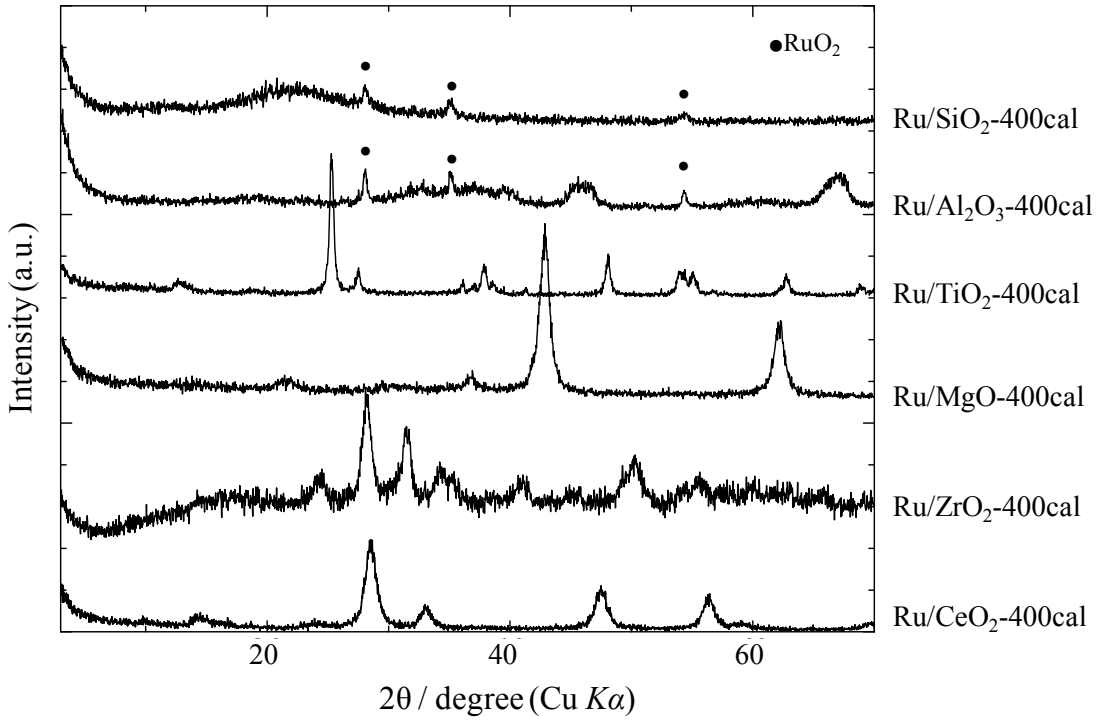


Figure 1. XRD patterns of supported Ru catalysts calcined at 400 °C.

K-edge extended X-ray absorption fine structure (EXAFS) spectra of supported Ru catalysts calcined at 400 ^{o}C and RuO_2 measured in transmission mode are shown in Figure 2. The oscillations of Ru catalysts supported on SiO_2, Al_2O_3 and TiO_2 resembled that of RuO_2. On the other hand, the oscillations of Ru/CeO_2 and Ru/MgO were very weak and completely different from that of RuO_2. This suggests that Ru species are highly dispersed on CeO_2 and MgO.

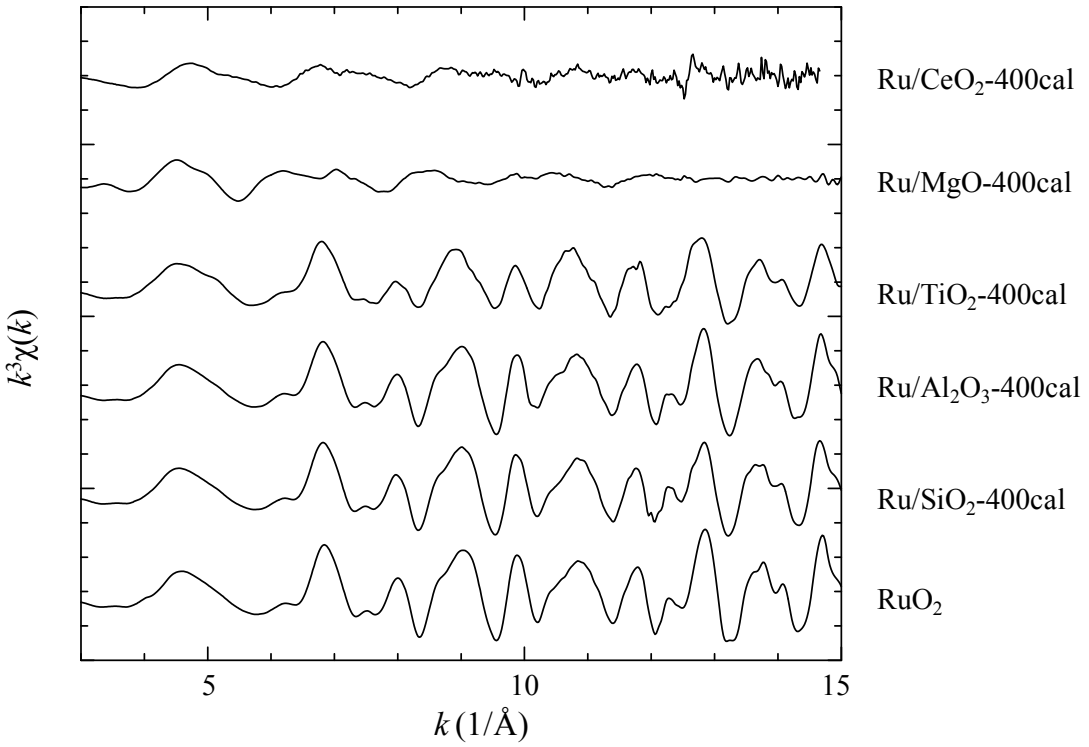


Figure 2. Ru K-edge oscillations of EXAFS spectra of supported Ru catalysts calcined at 400 ^{o}C.

Fourier transforms of EXAFS spectra are shown in Figure 3. The peaks at 2.0–4.0 Å due to a second coordination sphere in the spectrum of Ru/CeO_2 were very weak, presumably because of the presence of highly dispersed Ru species on CeO_2. On the other hand, the spectra of Ru catalysts on SiO_2, Al_2O_3 and TiO_2 closely resembled that of crystalline RuO_2. Ru species on MgO seems to be highly dispersed but were not effective for the catalytic reaction. This indicates that a characteristic feature other than the dispersion of Ru species must be important for the catalysis, as described below.

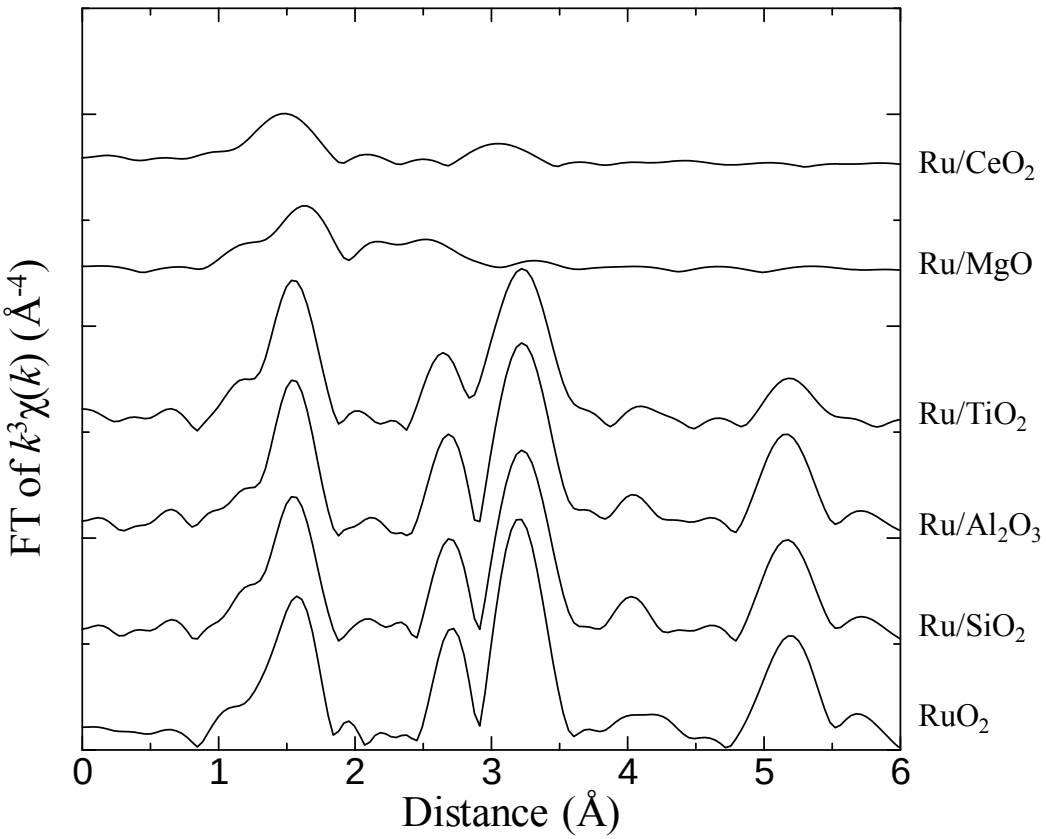


Figure 3. Ru K-edge FT of EXAFS spectra of supported Ru catalysts calcined at 400 ^{o}C.

As shown in Figure 4, the X-ray absorption near-edge structure (XANES) spectra of Ru catalysts supported on SiO_2, Al_2O_3 and TiO_2 are almost identical to that of rutile-type RuO_2. In contrast, the coordination environment of Ru species on CeO_2 was distinctly different: a pre-edge peak appeared at 22110 eV, indicating the formation of Ru(IV) species in a distorted coordination environment on CeO_2 [18]. Furthermore, the diffuse reflectance infrared Fourier transformed (DRIFT) spectrum of Ru/CeO_2 showed a characteristic peak at 980 cm^{-1} that could be assigned to the Ru=O vibration mode [18], while such a peak was not observed for RuO_2 and Ru catalysts supported on SiO_2, Al_2O_3, TiO_2 or MgO, as mentioned in previous chapters [6].

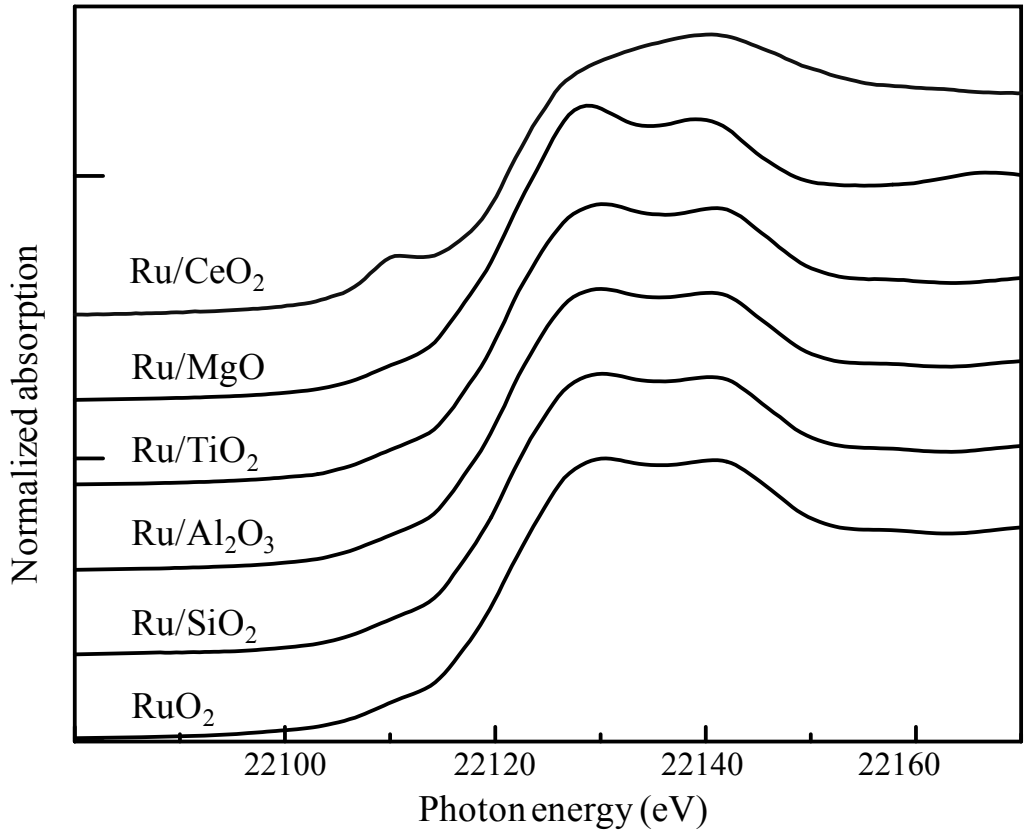


Figure 4. Ru K-edge XANES spectra of supported Ru catalysts calcined at 400 ^oC.

A pre-edge peak was observed in the XANES spectrum of Ru/ZrO_2 (Figure 5). The formation of Ru-oxo species on ZrO_2 has also been proposed previously [19,20]. These results suggest that the combination of Ru with CeO_2 or ZrO_2 creates the highly dispersed Ru(IV)-oxo species with a distorted coordination environment [5,18,19].

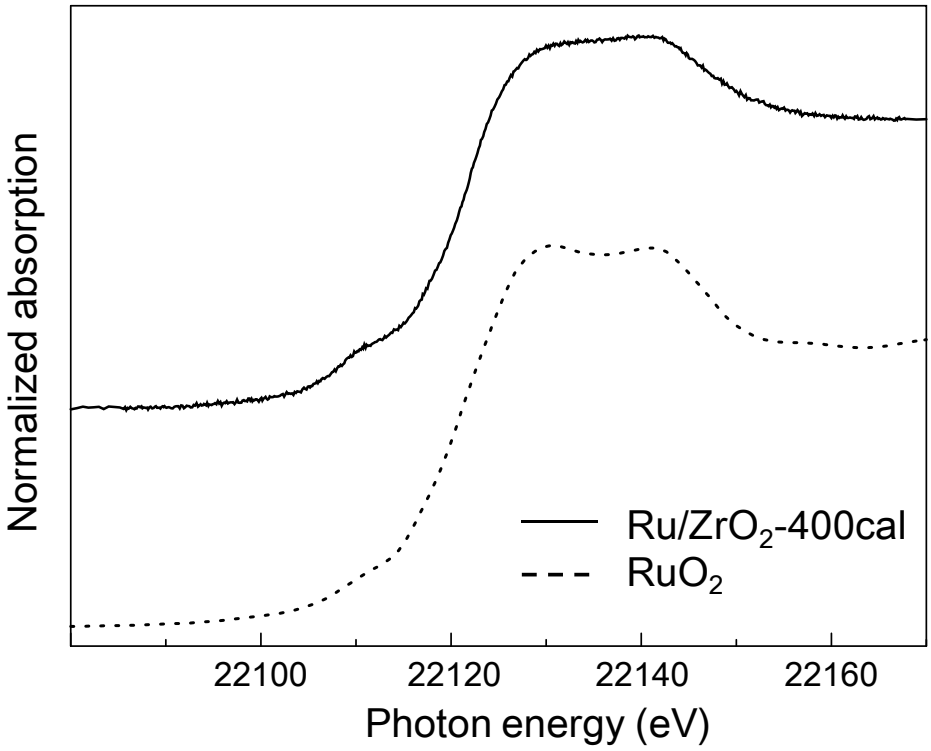


Figure 5. XANES spectra of Ru/ZrO_2 calcined at 400 ^oC and RuO_2.

The calcination temperature of the catalysts greatly affected the fine structure of Ru species on CeO_2 (Figure 6). The XANES spectrum of Ru/CeO_2 before calcination was very similar to that of $Ru(acac)_3$. In contrast, a pre-edge peak appeared in the spectra of Ru/CeO_2 calcined above 200 ^oC and the intensity increased with an increase in the calcination temperature.

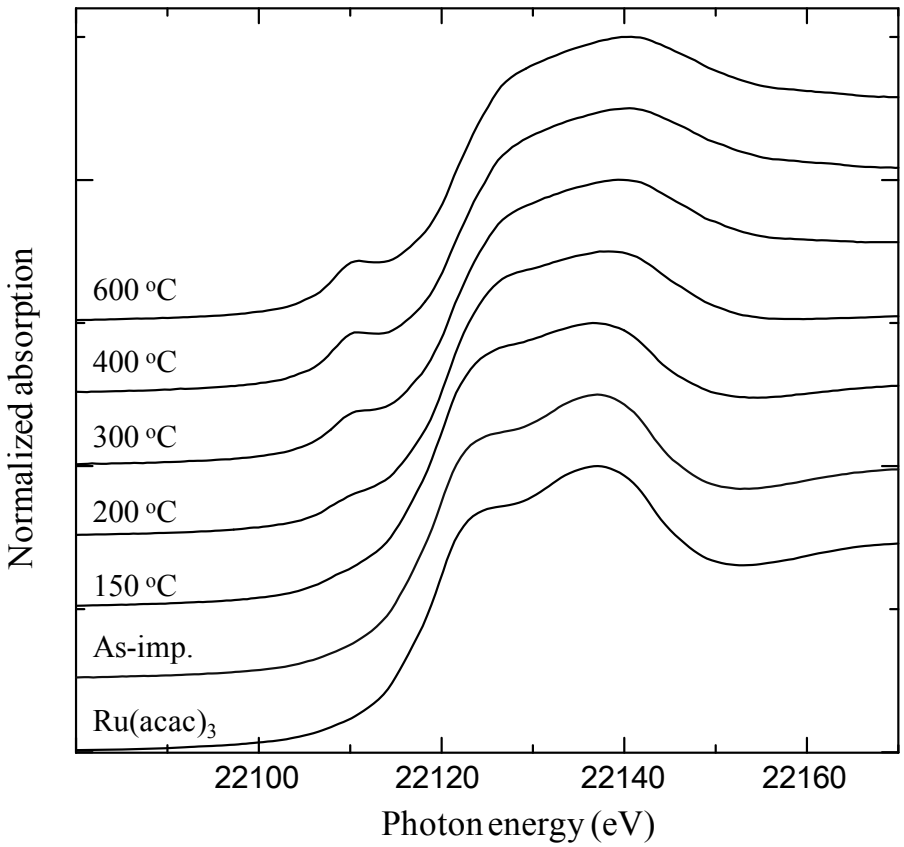


Figure 6. Ru K-edge XANES spectra of Ru/CeO_2 calcined at various temperatures.

TG-DTA profiles of as-impregnated Ru/CeO_2 in air showed an exothermic weight decrease at around 200 ^oC (Figure 7). The extent of the weight decrease is almost consistent with the weight of acetylacetonato ligands (5.6%).

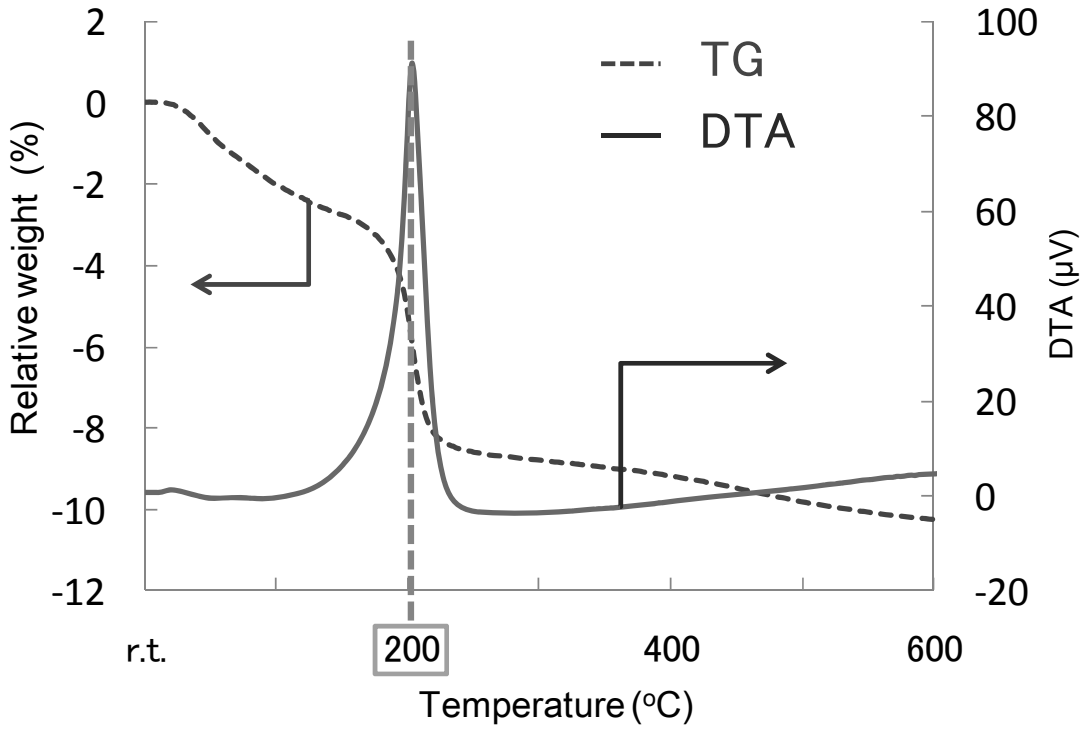


Figure 7. TG and DTA profiles of uncalcined Ru/CeO_2.

In DRIFT spectra of Ru/CeO_2 calcined above 200 ^oC, a peak due to Ru-oxo species was observed, while such a peak was not seen for catalysts calcined below 150 ^oC (Figure 8). These results indicated the presence of a $Ru(acac)_3$ or $Ru(acac)_3$-like species on uncalcined Ru/CeO_2 and the formation of a distorted Ru(IV)-oxo species after the combustion of acetylacetonato ligands.

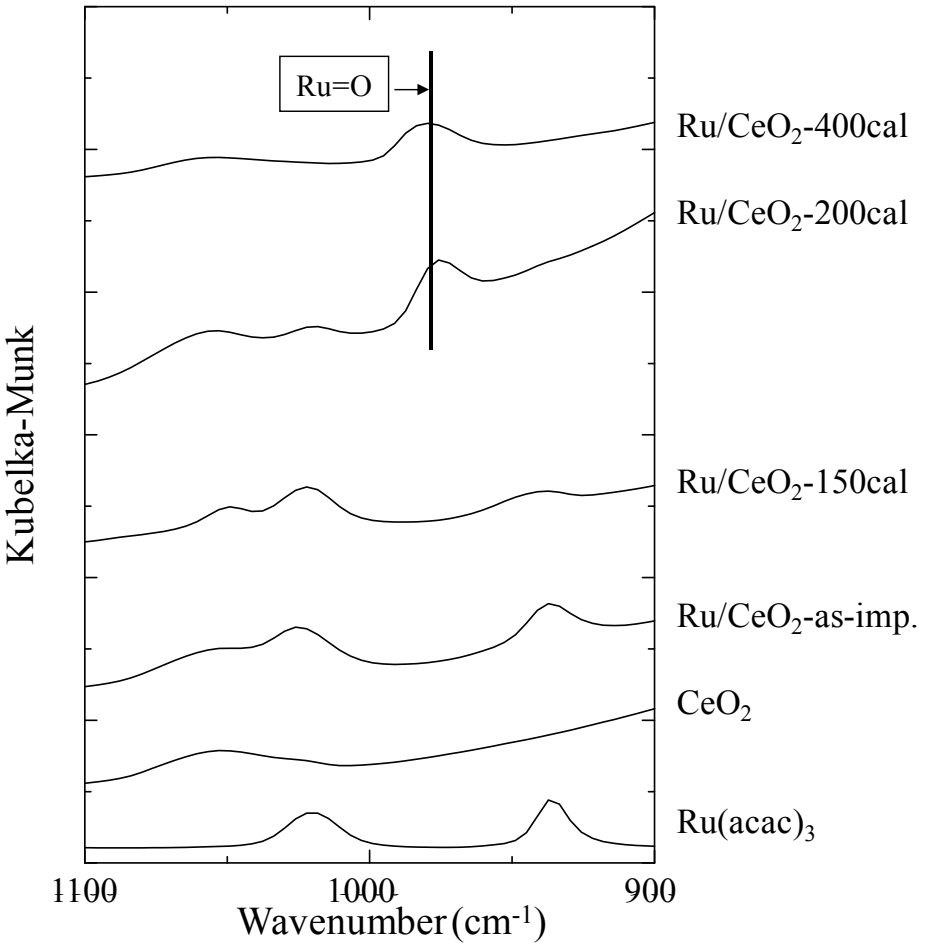


Figure 8. DRIFT spectra of Ru/CeO_2 calcined at various temperatures.

Figure 9 shows the yield of **3a** from the reaction at 110 ^{o}C for 1 h with Ru/CeO_2 calcined at various temperatures. Ru/CeO_2 before calcination did not show catalytic activity, and the reaction with Ru/CeO_2-150cal resulted in a low yield of **3a**. On the other hand, the reactions with the catalysts calcined above 300 ^{o}C proceeded efficiently, and Ru/CeO_2-600cal showed the highest activity. There was a good correlation between the catalytic activity and the intensity of the pre-edge peaks in XANES spectra (Figure 6), while calcination above 700 ^{o}C decreased the catalyst activity.

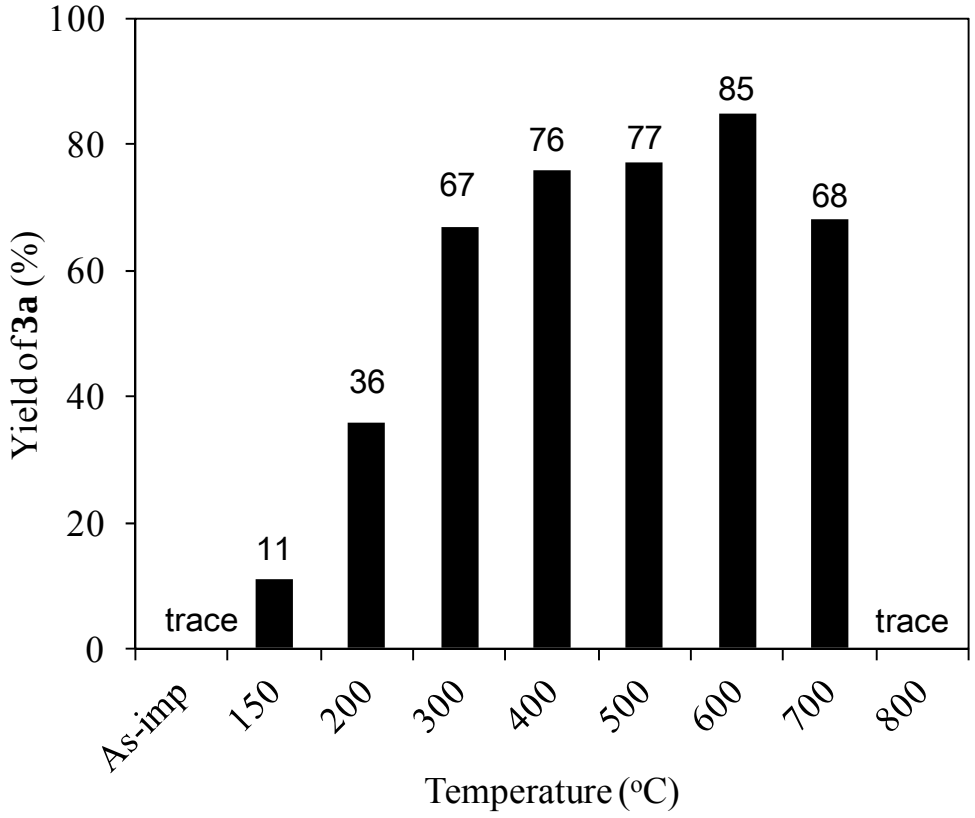


Figure 9. Effect of calcination tempreture of Ru/CeO_2 catalysts.

To investigate the state of Ru species during the reaction, XANES spectrum of the sample after the treatment of Ru/CeO_2-600cal with HCO_2Na in DMA at 110 ^oC for 15 min was obtained as shown in Figure 10. The absorption-edge of the XANES spectrum of the treated catalyst shifted to a lower energy, while Ru metal showed a completely different spectrum.

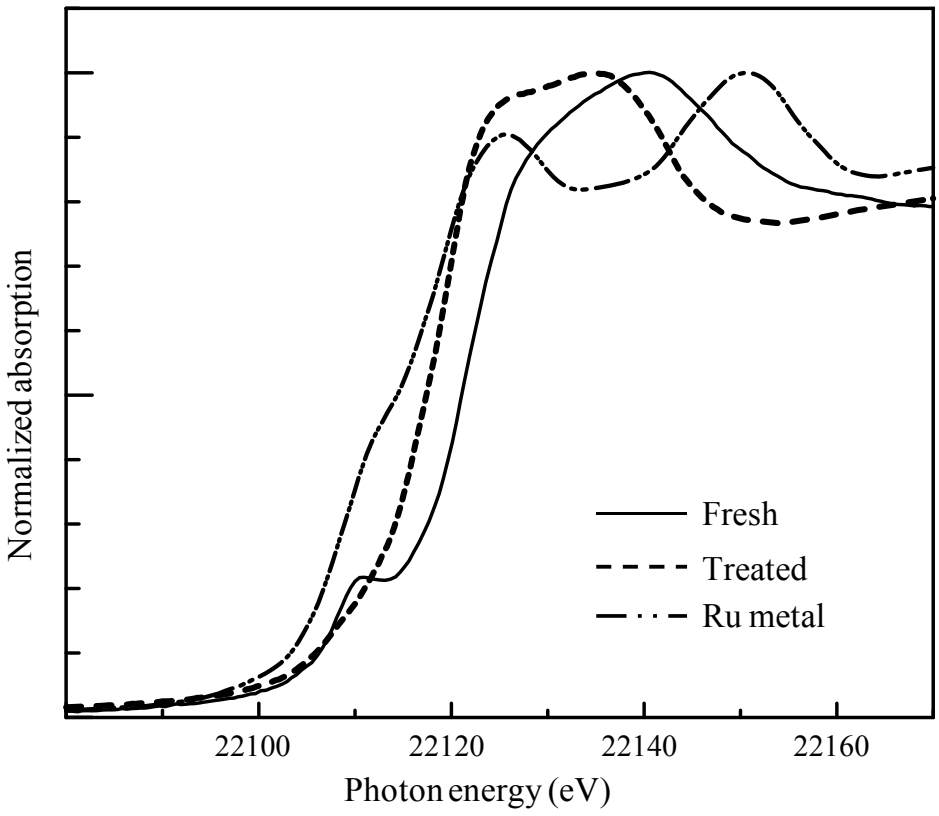


Figure 10. Ru K-edge XANES spectra of Ru/CeO_2-600cal before and after treatment in DMA.

Moreover, the peak due to Ru-oxo species in the DRIFT spectrum disappeared after the treatment (Figure 11). These results indicate that the Ru(IV) species are reduced to low-valent Ru species, but not to Ru metal, with a loss of a Ru=O bond at the initial stage of the reaction.

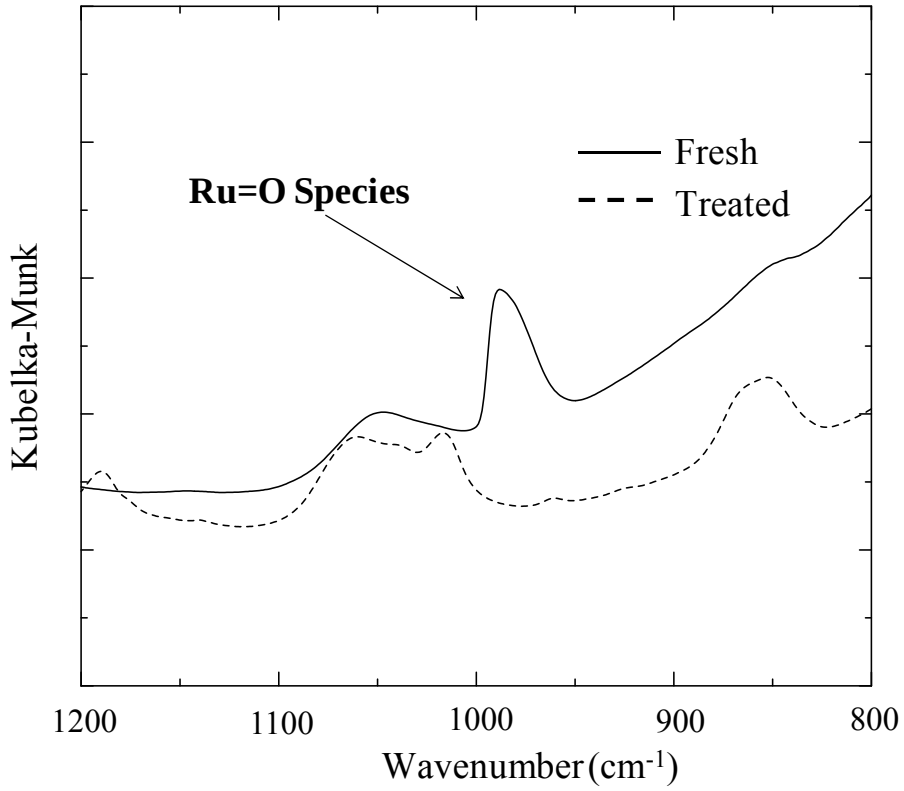
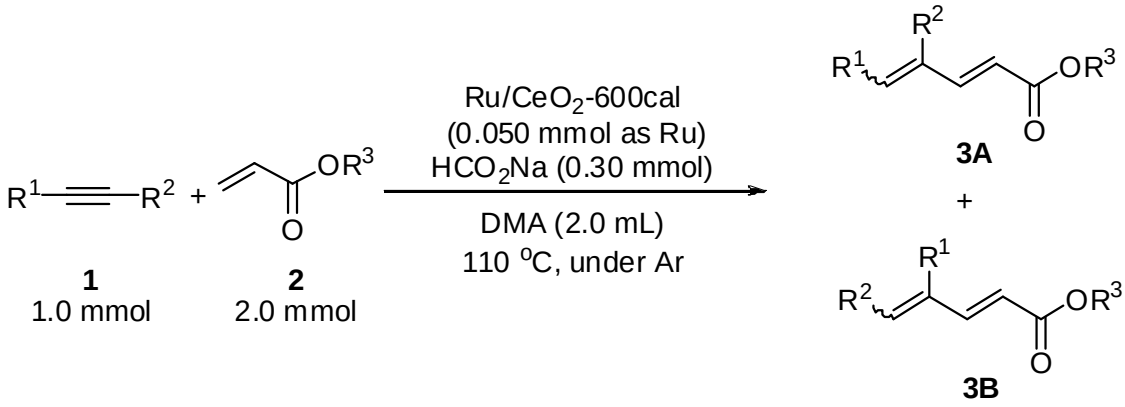


Figure 11. DRIFT spectra of Ru/CeO_2-600cal before and after treatment in DMA.

Considering the combined results of the catalytic reactions and spectroscopic analyses, the critical reason for the specific catalysis of Ru/CeO_2 or Ru/ZrO_2 is considered to be the formation of Ru(IV)-oxo species having a distorted coordination environment on the supports. The Ru(IV)-oxo species transform into catalytically-active low-valent Ru species under appropriate reaction conditions.

The results of the coupling reaction of various alkynes with acrylates using Ru/CeO_2-600cal are summarized in Table 3. The reaction of **1a** with **2a** was completed within 4 h even at 100 ^oC (entry 2). Ethyl, butyl and *tert*-butyl acrylate also gave the corresponding dienes in high yields (entries 3–5). With diarylacetylenes having MeO- or Cl substituent at para position of aromatic ring, the reactions proceeded smoothly to give the corresponding dienes in good yields. As for an unsymmetrical internal alkyne, 1-phenyl-1-propyne (**1b**) was examined and the corresponding dienes were obtained as a mixture of regioisomers (entry 8). The reaction with aliphatic internal alkynes, such as 4-octyne, gave a complex mixture of unidentified compounds.

Table 3. Reaction of internal alkynes with acrylate derivatives by Ru/CeO_2.



Entry	**1**	**2**	Time (h)	**3**	Yield (%)[a]	A : B
1	**1a** (R^1, R^2 = Ph)	**2a** (R^3 =Me)	2	**3a**	98[b] (93 : 7)	-
2[c]	**1a**	**2a**	4	**3a**	98[b] (95 : 5)	-
3[c]	**1a**	**2a** (R^3 = Et)	4	**3b**	86 (99 : 1)	-
4	**1a**	**2a** (R^3 = ^{n}Bu)	4	**3c**	87 (94 : 6)	-
5[d]	**1a**	**2a** (R^3 = ^{t}Bu)	2	**3d**	92 (85 : 15)	-
6	**1b** (R^1, R^2 = 4-MeO-C_6H_4)	**2a** (R^3 =Me)	6	**3e**	73 (99 : 1)	-
7	**1c** (R^1, R^2 = 4-Cl-C_6H_4)	**2a** (R^3 =Me)	24	**3f**	43 (72 : 28)	-
8[c]	**1d** (R^1 = Ph, R^2 = Me)	**2a** (R^3 =Me)	4	**3g**	76 (**3gA** = 95 : 5 **3gB** = 95 : 5)	87 : 13

[a] Isolated yields. [b] Determined by GLC. [c] Reaction at 100 °C. [d] Reaction at 120 °C.

After the reaction, the catalyst could be easily separated from the reaction mixture by centrifugation. The resulting solid was washed and then calcined at 600 ^{o}C to recover Ru/CeO_2 for reuse (eq. 1). As shown in Table 4, the solid catalyst could be recycled at least three times without a significant loss of the activity.

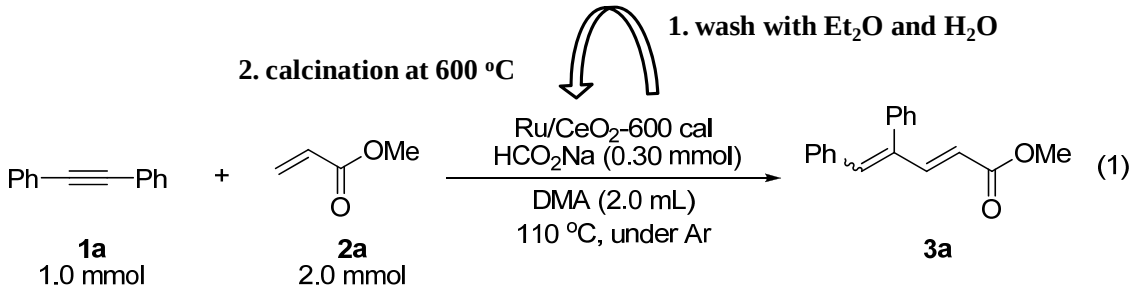


Table 4. Recycle of Ru/CeO_2 catalyst.

Entry	Recycle	Amount of catalyst (mg)	Yield of **3a** (%)[a]	
			2 h	3 h
1	Fresh	250	98	-
2	1st	244	98	-
3	2nd	236	95	-
4	3rd	226	85	94

[a] Determined by GLC.

Note that the amounts of Ru species that leached into the solution after the reactions in Table 3, entries 1 and 2 were only 0.00105 mmol and 0.00033 mmol (2.1% and 0.66% of Ru species in the fresh catalyst), respectively. On the other hand, hot filtration of solid Ru catalysts after the reaction for 45 min did not completely stop the reaction, which suggests that not only Ru species on the solid surface but also a very small amount of soluble Ru species is responsible for the reaction.

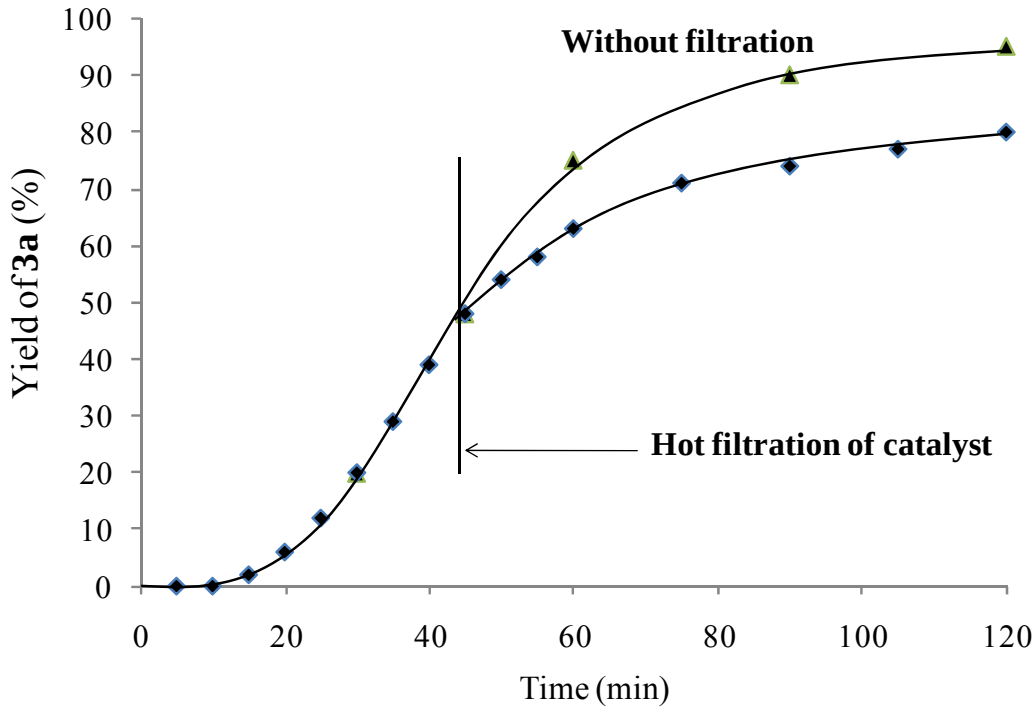
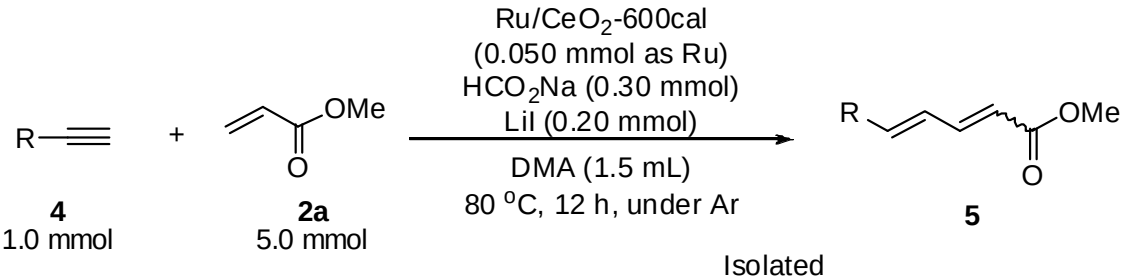


Figure 12. Hot filtration of Ru/CeO_2-600cal catalyst.

The coupling reactions of terminal alkynes with acrylate by the Ru/CeO_2 catalyst were also examined (Scheme 1). The addition of lithium iodide enhanced the yield of **5a** [11d], while the reaction in the absence of sodium formate did not give 1,3-dienes. Various terminal alkynes and 1,3-enyne could be used in the present catalytic system.



4
1.0 mmol

2a
5.0 mmol

5

	Isolated **5** : yield (*E* : *Z*)	
4a (R = Ph)	**5a :** 22% (80 : 20)	without LiI
4a (R = Ph)	**5a :** 0%	without HCO_2Na
4a (R = Ph)	**5a :** 76% (75 : 25)	
4b (R = 4-Me-C_6H_4)	**5b** : 61% (74 : 26)	
4c (R = 4-MeO-C_6H_4)	**5c** : 53% (76 : 24)	
4d (R = 3-thienyl)	**5d** : 54% (76 : 24)	
4e (R = 1-cyclohexenyl)	**5e** : 43% (79 : 21)	

Scheme 1. Reactions of terminal alkynes with methyl acrylate by Ru/CeO_2-600cal catalyst.

Several ruthenium complexes have been reported to catalyze the intermolecular couplings of two different alkenes [11e,21]. The coupling reactions of 2-norbornene with acrylates proceeded in the presence of Ru/CeO_2 catalysts together with sodium formate to give *exo*-alkenylated norbornanes in good yields with high *E* selectivities (>40 : 1) (Scheme 2).

6
5.0 mmol

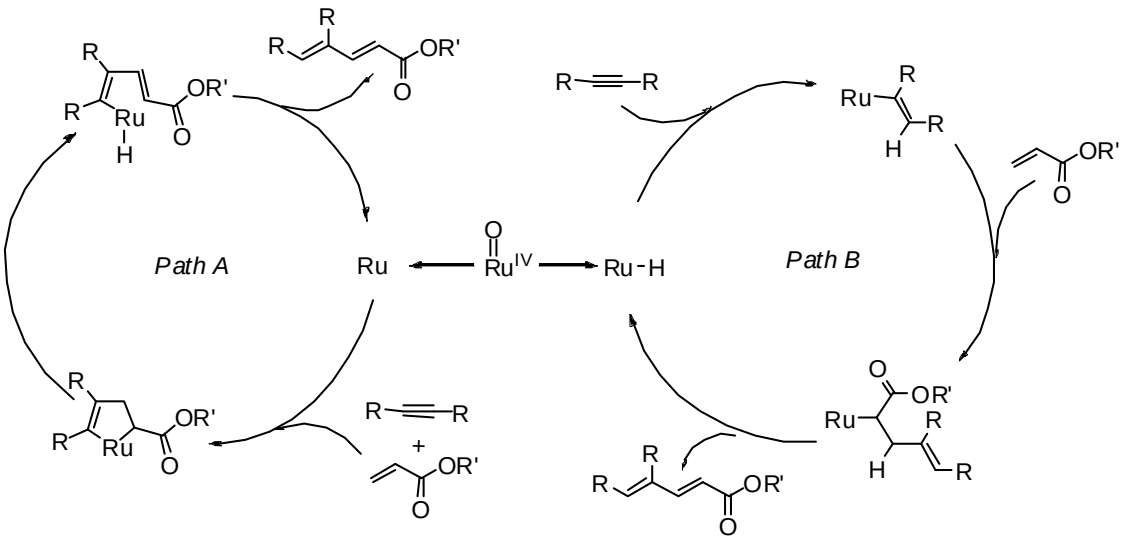
2
1.0 mmol

7

	GLC Yield
7a (R = Me)	66% (1 h)
7b (R = Et)	80% (2 h)
7c (R = ^{n}Bu)	76% (1 h)

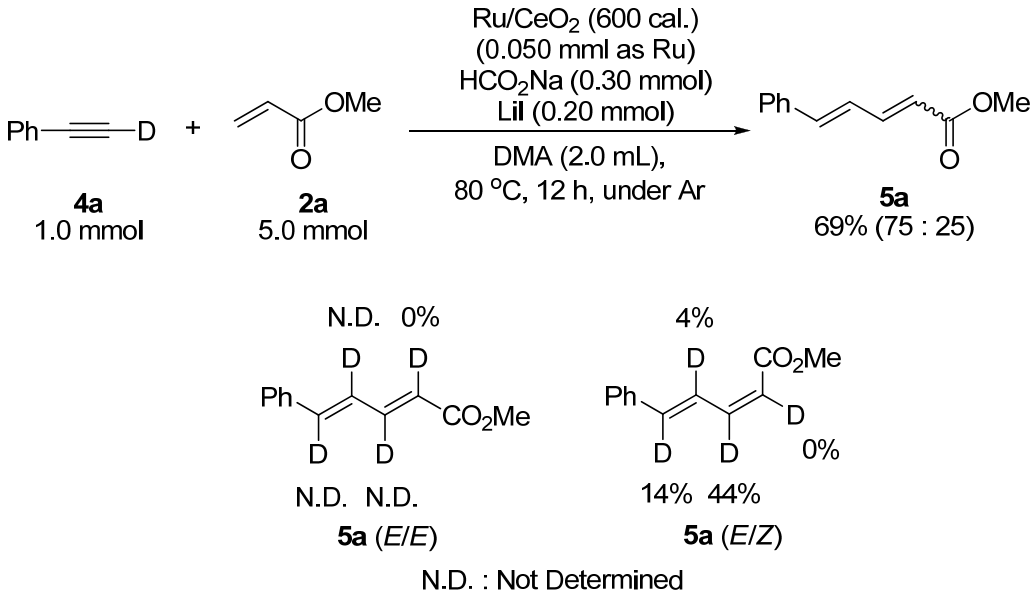
Scheme 2. Ru/CeO_2–catalyzed coupling of 2-norbornene with acrylates.

Several mechanisms for the coupling reaction of alkynes with alkenes have been proposed under homogeneous catalysis conditions. The first is a pathway *via* the formation of a ruthenacycle intermediate (Scheme 3, path A) [11a,f] and the second involves the generation of Ru hydride species, followed by the successive insertion of alkyne and alkene to Ru–H or Ru–C bonds (path B) [11e,22,23]. Although a mechanism that includes the activation of an sp^2 C–H bond of acrylate has also been proposed [11g,12c], the absence of the formation of a *cis* isomer at the α,β position of dienes and no isomerization in the course of the reaction suggest that the pathway via sp^2 C–H bond activation seems to be unlikely in the present case.



Scheme 3. Possible mechanisms for the coupling of alkynes with acrylates by low-valent Ru species generated from Ru(IV)-oxo species.

The reaction of *D*-labeled phenylacetylene with methyl acrylate was carried out (Scheme 4). After the reaction, 1,3-diene **5a** was isolated in a yield of 69%. Deuterium was scrambled in the β, δ and γ positions of **5a** (*E*/*Z*). This suggests the generation of a Ru hydride species in the course of the reaction. The relatively low *D*-content at δ position of **5a** suggests the absence of 1,2-migration during the reaction. Therefore, the reaction mechanism through a Ru-vinylidene species [11b] could be excluded.



Scheme 4. Deuterium-labeling experiment.

Although path A can not be completely excluded because of the formation of non-hydride low-valent Ru species from Ru dihydride species [17a], it is highly possible that Ru(IV)-oxo species in the presence of HCO_2Na transformed into Ru hydride species, which catalyzed the reaction *via* path B.

7.3 Conclusions

In this chapter, a highly efficient coupling of alkynes with acrylates by Ru/CeO_2 or Ru/ZrO_2 catalysts in the presence of sodium formate is described. The coupling of two different alkenes was also realized with this catalytic system. Spectroscopic studies suggested that Ru(IV)-oxo species with a distorted coordination environment on the inorganic supports, CeO_2 and ZrO_2, were transformed into catalytically active low-valent Ru species. The very simple and stable solid catalysts could be recycled without a significant loss of metal species from the oxide support.

7.4 Experimental

7.4.1 Materials and methods

All manipulations were performed under an argon atmosphere using standard Schlenk techniques. Ruthenium(III) acetylacetonate (Aldrich), di-μ-chlorobis[(*p*-cymene)chlororuthenium(II)] (Strem), ruthenium trichloride hydrate (Tanaka Kikinzoku), all of the acrylic compounds (TCI), 1-pheny-1-propyne (TCI), diphenylacetylene, all of the terminal alkynes, sodium formate, *N*,*N*-dimethylacetamide (Aldrich), cerium(III) nitrate hexahydrate, potassium hydroxide, and tetrahydrofuran (THF; Wako) were obtained commercially and used without further purification. Ceria was prepared by treating a solution of cerium(III) nitrate hexahydrate (12.6 g, 29 mmol) in 400 mL of deionized water with 40 mL of 3M KOH aqueous solution with stirring for 1 h at room temperature. The resulting precipitates were collected by centrifugation, washed thoroughly with deionized water and then air-dried overnight at 80 ^{o}C. The product was heated in a box furnace at a rate of 10 ^{o}C min^{-1} and maintained at 400 ^{o}C for 30 min to afford ceria in an excellent ceramic yield. Magnesium oxide was prepared from magnesium nitrates by a method similar to that used to obtain ceria. Zirconia (JRC-ZRO-3), titania (JRC-TIO-4), γ-alumina (JRC-ALO-8) and silica (Cabosil) were used as received.

7.4.2 Physical and Analytical Measurements

The products of the catalytic runs were analyzed by GC-MS (Shimadzu GC-MS Parvum 2, Zebron ZB-1 capillary column, i.d. 0.25 mm, length 30 m, at 50–250 ^{o}C) and gas chromatography (GL Sciences GC353, Inertcap 17 capillary column, i.d. 0.25 mm, length 30 m at 50–250 ^{o}C). NMR spectra were recorded on a JEOL JNM-EX-400 (FT,

400 MHz (^{1}H), 100 MHz (^{13}C)) instrument. Chemical shifts (δ) are referenced to $SiMe_4$. High-resolution mass spectra (FAB) were recorded on a JEOL SX102A spectrometer with *m*-nitrobenzyl alcohol (*m*-NBA) as a matrix. IR spectra were recorded using a Nicolet Magna-IR 560 FT-IR spectrometer.

The solid catalysts were analyzed by XRD, nitrogen gas adsorption, FTIR and XAFS. X-ray powder diffraction analyses were performed using Cu *K*α radiation and a carbon monochromator (XRD: XD-D1, Shimadzu). Nitrogen adsorption isotherms were obtained with a computer-controlled automatic gas sorption system (Quantachrome NOVA 4200e). Samples were degassed at 300 ^{o}C for 2 h just before the measurements. Diffuse reflectance infrared Fourier transformed (DRIFT) spectra was recorded using a Nicolet Magna-IR 560 FT-IR spectrometer with DRIFT optical configuration. Ru K-edge XAFS measurements were performed at the BL01B1 beam line in the SPring-8 operated at 8 GeV using a Si(311) two-crystal monochromator. XAFS spectra were taken at room temperature. XANES and EXAFS were analyzed using the REX2000 version 2.5 program (Rigaku). Leaching of ruthenium species from the catalysts during the reaction was investigated by ICP atomic emission spectroscopic analysis with a Shimadzu ICPS-1000III.

7.4.3 Preparation of supported Ru catalysts

Supported catalysts were prepared by the impregnation method. 1.0 g of a support was added to a solution of $Ru(acac)_3$ (79.5 mg, 0.20 mmol) in 10 mL of THF in air at room temperature. After impregnation, the resulting powder was calcined in air for 30 min to afford the Ru(2.0 wt%)/Support catalyst.

7.4.4 General procedure for coupling of alkynes with acrylates by Ru/CeO_2 catalysts

Diphenylacetylene **1a** (178 mg, 1.0 mmol), ethyl acrylate **2b** (0.20 mL, 2.0 mmol), sodium formate (20.4 mg, 0.30 mmol) and *N*,*N*-dimethylacetamide (2.0 mL) were placed in a glass Schlenk tube under an argon atmosphere together with 250 mg of the Ru/CeO_2-600cal (0.050 mmol as Ru). The reaction mixture was stirred at 100 ^oC for 4 h on a hot stirrer equipped with a cooling block. After the reaction, the solution was separated from the reaction mixture by centrifugation and concentrated under reduced pressure. The products were isolated by column chromatography (hexane : ethyl acetate = 10:1, v/v) to give the product **3b** as a white solid; yield: 239 mg (86%).

7.4.5 Hot filtration tests

A 20 mL Schlenk tube was charged with diphenylacetylene **1a** (178 mg, 1.0 mmol), methyl acrylate **2a** (0.18 mL, 2.0 mmol), Ru/CeO_2-600cal catalyst (250 mg, 0.050 mmol as Ru), sodium formate (20.4 mg, 0.30 mmol) and DMA (2.0 mL) together with an internal standard (*o*-terphenyl, *ca*. 50 mg) under an argon atmosphere. After the reaction was allowed to proceed for 45 min at 110 ^oC, the mixture was filtered through a 0.45 μm syringe filter (Millipore Millex LH) into another preheated Schlenk tube. The

filtrate was stirred at 110 ^{o}C. The conversion and yields of the product after filtration were followed by GC and GC-MS analyses.

7.4.6 Characterization of new compounds (3e, 3f, 5d, 5e)

Methyl 4,5-bis(4-methoxyphenyl)penta-2,4-dienoate (2*E*/4*Z*) (3e): white solid; m.p. 104 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.66 (d, J = 16.1, 1H), 7.06 (d, J = 8.8 Hz, 2H), 6.94 (m, 4H), 6.84 (s, 1H), 6.67 (d, J = 8.8 Hz, 2H), 5.47 (d, J = 15.1, 1H) , 3.85 (s, 3H) , 3.74 (s, 3H) ,3.71 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 167.9, 159.6, 159.1, 150.6, 138.6, 137.2, 131.6, 130.4, 129.2, 128.6, 118.5, 114.7, 113.7, 55.3, 55.2, 51.4. FT-IR (neat) 1705 cm^{-1}. HRMS: Calculated for $C_{20}H_{20}O_4$ (M): 324.1362; found: 314.1368.

Methyl 4,5-bis(4-chlorophenyl)penta-2,4-dienoate (2*E*/4*Z*) (3f): white solid; m.p. 114 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.64 (d, J = 14.8, 1H), 7.41 (d, J = 8.8 Hz, 2H), 7.10 (m, 4H), 6.87 (m, 3H), 5.48 (d, J = 15.6, 1H) , 3.73 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 167.4, 148.9, 138.8, 137.5, 134.9, 134.3, 133.8, 131.1, 130.6, 129.6, 128.6, 120.4, 51.6. FT-IR (neat) 1705 cm^{-1}. HRMS: Calculated for $C_{18}H_{14}Cl_2O_2$ (M): 332.0371; found: 312.0369.

Methyl 5-(thiophen-3-yl)penta-2,4-dienoate (2*E*/4*E*) (5d): Orange solid; m.p. 99 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.41 (dd, J = 15.1, 11.2 Hz, 1H), 7.33–7.27 (m, 3H), 6.90 (d, J = 15.6 Hz, 1H), 6.69 (dd, J = 15.5, 11.2 Hz, 1H), 5.96 (d, J = 15.6 Hz, 1H), 3.76 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 167.5, 145.0, 139.1, 134.3, 126.7, 126.2, 125.3, 124.9, 120.3, 51.5. FT-IR (neat) 1706 cm^{-1}. HRMS: Calculated for $C_{10}H_{11}O_2S$ (M+H): 195.0480; found: 195.0475.

Methyl 5-cyclohexenylpenta-2,4-dienoate (2*E*/4*E*) (5e): Orange liquid; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.33 (dd, J = 15.1, 11.2 Hz, 1H), 6,54 (d, J = 15.1, 1H), 6.21 (dd, J = 15.1, 11.2 Hz, 1H), 5.98 (m, 1H), 5.85 (d, J = 15.1 Hz, 1H), 3.74 (s, 3H), 2.18 (m, 4H), 1.69 (m, 2H), 1.61 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 167.7, 145.8, 144.6, 135.8, 135.3, 122.8, 119.1, 51.4, 26.4, 24.3, 22.2. FT-IR (neat) 1722 cm^{-1}. HRMS: Calculated for $C_{12}H_{16}O_2$ (M): 192.1150; found: 192.1144.

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Chapter 8

Intermolecular hydroacylation of alkynes in the presence of recyclable Ru/CeO_2 catalysts

8.1 Introduction

Carbon–carbon bond-forming reactions that involve the activation and subsequent functionalization of C–H bonds catalyzed by transition-metals are the most important reactions in current organic chemistry [1]. The intra- and inter-molecular hydroacylation of C–C multiple bonds is a promising method for the preparation of ketones and conjugated enones because of its inherent 100% atom-efficiency [2]. Although transition-metal catalysts can cleave C–H bonds of formyl groups to give acyl–metal species which are key intermediates in catalytic hydroacylation, these intermediates often undergo rapid decomposition into metal carbonyl species and reduced molecules before coupling across C–C multiple bonds. To suppress the decarbonylation and to obtain hydroacylation products in high yields, various strategies have been developed: a) chelation-controlling with S or O substituents [3], b) imination of aldehydes, followed by C–C coupling and hydrolysis [4], c) use of pressurized of CO [5], and d) an alternative reaction pathway through the coupling of allyl–metal species with aldehydes [6]. However, the development of new catalytic systems that could broaden the scope of substrates for intermolecular hydroacylation is still a challenge.

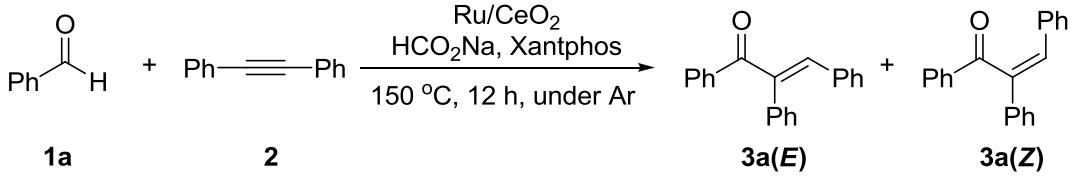
On the other hand, highly selective organic transformation with recyclable solid catalysts has attracted much attention from the perspective of green and sustainable chemistry [7]. As described in the previous chapters, CeO_2-supported Ru catalysts (Ru/CeO_2) showed excellent catalytic performance and recyclability for various synthetic reactions such as the direct arylation of aromatic C–H bonds and the intermolecular coupling of alkynes with alkenes [8]. These results indicate that the Ru/CeO_2 is an attractive catalyst candidate for new synthetic reactions.

In this chapter, the catalytic intermolecular hydroacylation of alkynes in the presence of solid Ru/CeO_2 is described. Various aromatic aldehydes with or without coordinating groups can be used in the present catalytic system. The solid Ru catalysts are recyclable without a significant loss of activity.

8.2 Results and discussion

The intermolecular coupling of aromatic aldehyde (**1a**) with diphenylacetylene (**2**) took place in the presence of a catalytic amount of Ru/CeO_2 (5.0 mol% as Ru) together with 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (Xantphos) and HCO_2Na in *N*,*N*-dimethylacetamide (DMA) at 150 ^oC under an Ar atmosphere to give the corresponding conjugated enone **3a** in a yield of 52% (Table 1, entry 1). The reaction in the absence of either HCO_2Na or Xantphos did not take place at all (entries 2 and 3). Among other phosphorous ligands examined [9], PPh_3, dppe, dppp, dppb, dpppe, dppf, *rac*-BINAP, DPEphos and ^{t}Bu-Xantphos were not effective (entries 4–11). As a reaction solvent, DMA, *N*,*N*-dimethylformamide (DMF) and *N*-methyl-2-pyrrolidone (NMP) were suitable (entries 1, 12 and 13). In contrast, toluene, mesitylene, 1,4-dioxane and diglyme were totally ineffective (entries 1 and 14–17).

Table 1. Effects of phosphines and solvents on Ru/CeO_2-catalyzed hydroacylation.[a]



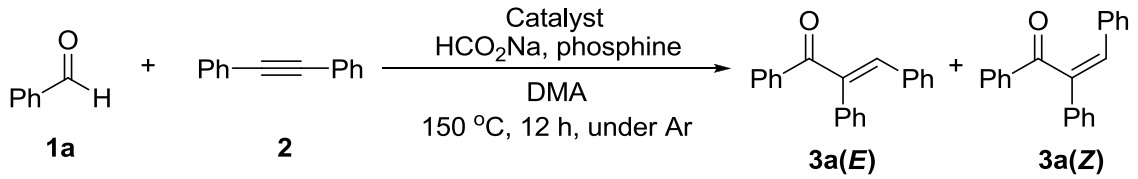
1a **2** **3a(*E*)** **3a(*Z*)**

Entry	Phosphine	Solvent	Yield of **3a** (%)[b]	Sel. (*E* : *Z*)[b]
1	Xantphos	DMA	52	64 : 36
2[c]	Xantphos	DMA	0	-
3	-	DMA	0	-
4	PPh_3	DMA	0	-
5	dppe	DMA	0	-
6	dppb	DMA	0	-
7	dpppe	DMA	0	-
8	dppf	DMA	0	-
9	*rac*-BINAP	DMA	0	-
10	DPEphos	DMA	0	-
11	^{t}Bu-Xantphos	DMA	0	-
12	Xantphos	DMF	50	64 : 36
13	Xantphos	NMP	40	64 : 36
14	Xantphos	toluene	0	-
15	Xantphos	mesitylene	0	-
16	Xantphos	1,4-dioxane	0	-
17	Xantphos	diglyme	0	-

[a] *Reaction conditions*: **1a** (0.50 mmol), **2** (1.5 mmol), solvent (2.0 mL), Ru/CeO_2 125 mg (0.025 mmol as Ru), HCO_2Na (0.15 mmol), phosphine (0.050 mmol as P) at 150 °C for 12 h under Ar. [b] Determined by GLC. [c] Without HCO_2Na.

The effects of various transition-metal catalysts on the intermolecular hydroacylation of **2** with **1a** were examined (Table 2). Ru/CeO_2 and Ru/ZrO_2 catalysts showed activities for the present reaction, whereas **3a** was not obtained at all with other solid Ru catalysts supported on SiO_2, Al_2O_3, TiO_2 or MgO (entries 1–6). Among homogeneous Ru complex catalysts, $[RuCl_2(p\text{-cymene})]_2$ and $[RuCl_2(CO)_3]_2$ showed moderate activities under the present reaction conditions (entries 7 and 8). On the other hand, as with Ru/CeO_2, these Ru complex catalysts showed no activities without HCO_2Na (entry 9). Darses and co-workers reported that the reaction of $[RuCl_2(p\text{-cymene})]_2$ with formate salts gave RuH_2 species, which are easily reduced to Ru(0) species by the reaction of unsaturated compounds [10]. In the presence of other transition-metal complex catalysts, $Ru_3(CO)_{12}$, $RuHCl(CO)(PPh_3)_3$, $[RhCl(cod)]_2$, $[IrCl(cod)]_2$ and $Pd(OAc)_2$, the reaction of **1a** with **2** resulted in low yields of **3a** (entries 7–13).

Table 2. Effects of catalysts on the intermolecular hydroacylation of **2a**.[a]

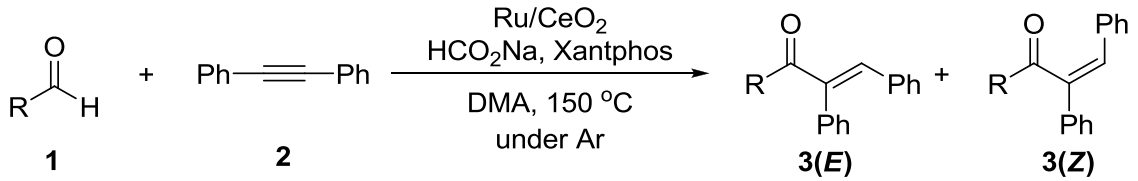


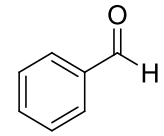
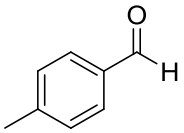
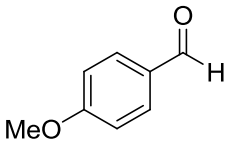
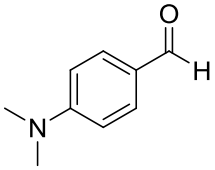
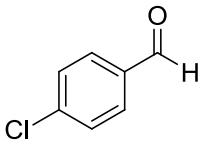
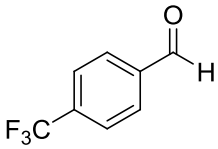
Entry	Catalyst	Time	Yield of **3a** (%)[b]	Sel. (*E* : *Z*)[b]
1	Ru/CeO_2	12	52	64 : 36
2[c]	Ru/ZrO_2	12	36	64 : 36
3	Ru/SiO_2	12	0	-
4	Ru/Al_2O_3	12	0	-
5	Ru/TiO_2	12	0	-
6	Ru/MgO	12	0	-
7	$[RuCl_2(CO)_3]_2$	3	41	64 : 36
8	$[RuCl_2(p\text{-cymene})]_2$	3	49	64 : 36
9[c]	$[RuCl_2(p\text{-cymene})]_2$	3	0	-
10[c]	$Ru_3(CO)_{12}$	12	<5	-
11[c]	$RuHCl(CO)(PPh_3)_3$	12	0	-
12	$[RhCl(cod)]_2$	12	<5	-
13	$[IrCl(cod)]_2$	12	<5	-
14	$Pd(OAc)_2$	12	6	64 : 36

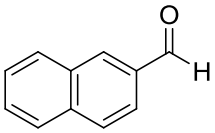
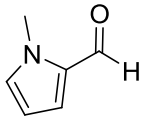
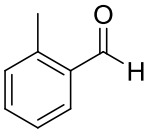
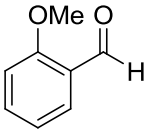
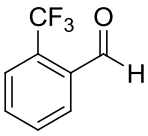
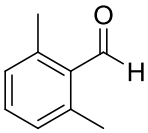
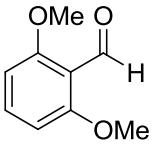
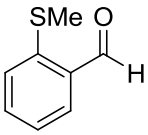
[a] *Reaction conditions*: **1a** (0.50 mmol), **2** (1.5 mmol), solvent (2.0 mL), catalyst (0.025 mmol as metal), HCO_2Na (0.15 mmol), phosphine (0.050 mmol as P) at 150 °C for 12 h under Ar. [b] Determined by GLC. [c] Without HCO_2Na.

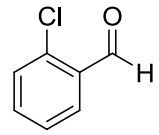
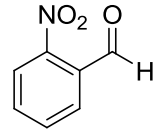
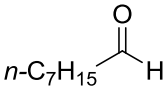
Under the optimized reaction conditions, the intermolecular hydroacylation of **2** with various aldehydes was examined in the presence of the solid Ru/CeO_2 catalyst (Table 3). The reaction of **1a** with **2** went to completion within 6 h when an increased amount of ligand (Xantphos/Ru = 2) was used (entry 1). From *p*-substituted aromatic aldehydes, the corresponding conjugated enones **3b**–**3f** were obtained in moderate yields (entries 2–5). 2-Naphthaldehyde and *N*-methyl-2-pyrrolecarbaldehyde could be used (entries 7 and 8). On the other hand, the reactions of aromatic aldehydes with substituents at the *ortho*-position gave the desired products (**3i**–**3k**) in high yields (entries 9–11). From aldehydes with substituents at both the *ortho*-positions of aromatic rings, the conjugated enones **3l** and **3m** were obtained in high yields and with excellent *E* selectivities (entries 12 and 13). In contrast, an *ortho*-S-substituted aldehyde (**1n**) did not participate in the present catalytic reaction (entry 14), although in Rh-complex-catalyzed reactions the methyl sulfide group functions as a good coordinating substituent to afford the hydroacylation products in high yields [3c–f,h,i,k,l]. Unfortunately, aromatic aldehydes with a chloro or nitro substituent at the *ortho*-position and simple aliphatic aldehydes, such as 1-octanal, could not be used in the present catalytic system (entries 15–17).

Table 3. Ru/CeO_2-catalyzed hydroacylation of **2** with various aldehydes.[a]



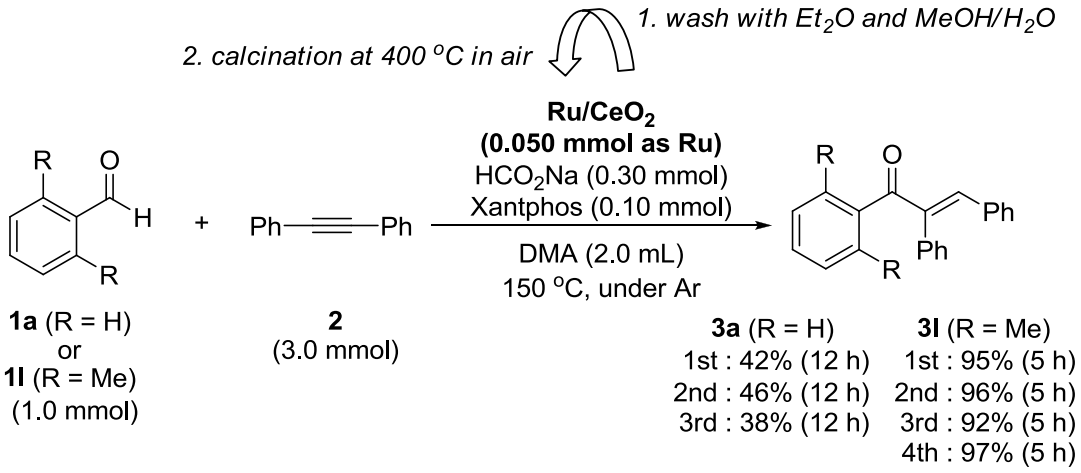
Entry	**1**	Time (h)	Product	Yield of **3** (%)[b]	Sel. (*E* : *Z*)[c]
1	 **1a**	6	**3a**	52	64 : 36
2	 **1b**	12	**3b**	58	68 : 36
3	 **1c**	12	**3c**	46	68 : 32
4	 **1d**	12	**3d**	53	57 : 43
5	 **1e**	12	**3e**	43	75 : 25
6	 **1f**	12	**3f**	19	53 : 47

7	 **1g**	12	**3g**	44	65 : 35
8	 **1h**	12	**3h**	54	60 : 40
9	 **1i**	12	**3i**	72	72 : 28
10	 **1j**	5	**3j**	80	70 : 30
11	 **1k**	18	**3k**	64	98 : 2
12	 **1l**	5	**3l**	86	99 : 1
13	 **1m**	5	**3m**	81	98 : 2
14	 **1n**	12	**3n**	0	-

15	 **1o**	12	**3o**	0	-
16	 **1p**	12	**3p**	0	-
17	 **1q**	12	**3q**	0	-

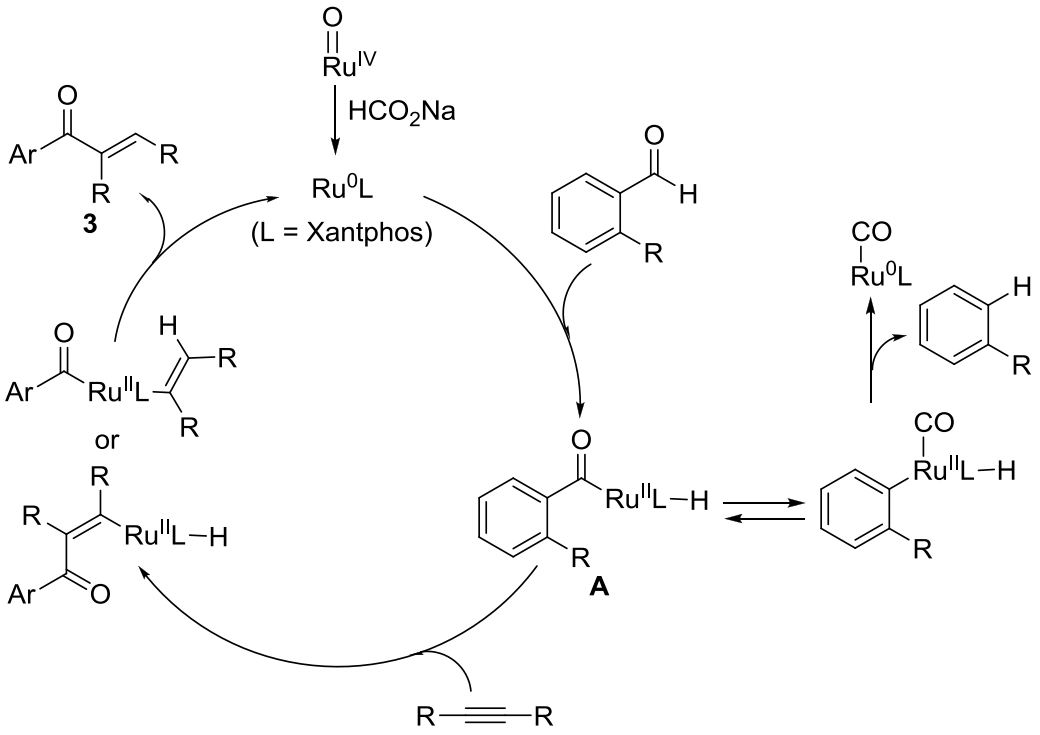
[a] *Reaction conditions*: **1** (0.50 mmol), **2** (1.5 mmol), DMA (2.0 mL), Ru/CeO_2 (0.025 mmol as Ru), HCO_2Na (0.15 mmol), Xantphos (0.050 mmol, 0.10 mmol as P) under Ar. [b] Isolated yield. [c] Determined by ^1H NMR.

One of the most advantageous features of solid catalysts is their high recyclability. After the reaction of **1a** or **1l** with **2a**, the solid Ru catalyst was separated from the reaction mixture by centrifugation and washed with diethyl ether and water/methanol. The resulting powder was calcined in air at 400 ^{o}C for 30 min to recover Ru/CeO_2 for subsequent catalytic runs. As shown in Scheme 1, the solid Ru/CeO_2 continued to show catalytic activity and gave **3a** and **3l** without significant decreases in yields for at least three times (Scheme 1). Note that the amount of Ru species leached into the solution after the reaction of **1l** with **2** by the fresh Ru/CeO_2 catalyst was only 2.0% of the Ru species in the fresh catalyst.



Scheme 1. Recycling of the Ru/CeO_2 catalyst.

Although the reaction mechanisms in the present Ru/CeO_2 catalytic system are not yet fully understood, a plausible mechanism is shown in Scheme 2 [2,5h,11]. An X-ray absorption fine structure (XAFS) study revealed that Ru(IV) species on CeO_2 were transformed into low-valent Ru species, probably Ru(II) species, by treatment with HCO_2Na and Xantphos in DMA at 150 ^oC (Figure 1). In the course of the reaction, the Ru(II) species could be reduced by alkynes to Ru(0) species with Xantphos ligand [12], which cleaved the formyl C–H bonds to give acyl–Ru intermediate **A**. Alkynes then inserted into Ru–C or Ru–H bonds, and reductive elimination gave conjugate enones **3**. The decarbonylation from intermediate **A** may be suppressed by the steric hindrance of substituents on the *ortho*-position of aromatic aldehydes and/or that of Xantphos ligand.



Scheme 2. Plausible reaction mechanism for intermolecular hydroacylation by Ru/CeO_2.

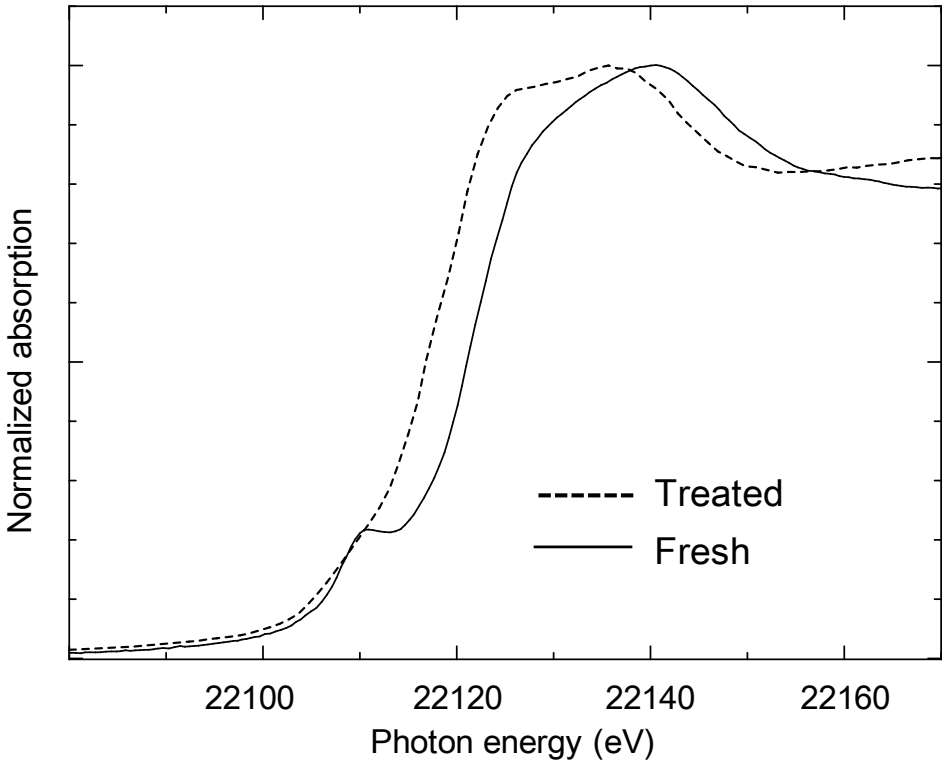


Figure 1. X-ray absorption near-edge structure of Ru/CeO_2.

8.3 Conclusions

This chapter described the Ru/CeO_2/Xantphos-catalyzed intermolecular hydroacylation of alkynes. The reaction of aldehydes with or without coordinating groups gives the corresponding conjugated enones in good yields. In particular, aromatic aldehydes with substituents at the *ortho*-positions of aromatic rings are transformed to the products in high yields. The present solid Ru catalytic system shows high environmental compatibility because of their high recyclability and the very low contamination of the products by metallic species.

8.4 Experimental

8.4.1 Materials and methods

All manipulations were performed under an argon atmosphere using standard Schlenk techniques. Ruthenium(III) acetylacetonate (Aldrich), all of the aldehydes (TCI), diphenylacetylene, sodium formate, *N*,*N*-dimethylacetamide (Aldrich), cerium(III) nitrate hexahydrate, potassium hydroxide, and tetrahydrofuran (THF; Wako) were obtained commercially and used without further purification. Ceria was prepared by treating a solution of cerium(III) nitrate hexahydrate (12.6 g, 29 mmol) in 400 mL of deionized water with 40 mL of 3M KOH aqueous solution with stirring for 1 h at room temperature. The resulting precipitates were collected by centrifugation, washed thoroughly with deionized water and then air-dried overnight at 80 ^{o}C. The product was heated in a box furnace at a rate of 10 ^{o}C min^{-1} and maintained at 400 ^{o}C for 30 min to afford ceria in an excellent ceramic yield. Magnesium oxide was prepared from magnesium nitrates by a method similar to that used to obtain ceria. Zirconia (JRC-ZRO-3), titania (JRC-TIO-4), γ-alumina (JRC-ALO-8) and silica (Cabosil) were used as received.

8.4.2 Physical and analytical measurements

The products of the catalytic runs were analyzed by GC-MS (Shimadzu GC-MS Parvum 2, Zebron ZB-1 capillary column, i.d. 0.25 mm, length 30 m, at 50–250 ^{o}C) and gas chromatography (GL Sciences GC353, Inertcap 17 capillary column, i.d. 0.25 mm, length 30 m at 50–250 ^{o}C). NMR spectra were recorded on a JEOL JNM-EX-400 (FT, 400 MHz (^{1}H), 100 MHz (^{13}C)) instrument. Chemical shifts (δ) are referenced to $SiMe_4$.

High-resolution mass spectra (FAB) were recorded on a JEOL SX102A spectrometer with *m*-nitrobenzyl alcohol (*m*-NBA) as a matrix. IR spectra were recorded using a Nicolet Magna-IR 560 FT-IR spectrometer.

The solid catalysts were analyzed by XAFS. Ru K-edge XAFS measurements were performed at BL01B1 beam line at SPring-8 operated at 8 GeV using a Si(311) two-crystal monochromator. XAFS spectra were taken at room temperature. XANES and EXAFS were analyzed using the REX2000 version 2.5 program (Rigaku). Leaching of ruthenium species from the catalysts during the reaction was investigated by ICP atomic emission spectroscopic analysis with a Shimadzu ICPS-1000III.

8.4.3 Preparation of supported Ru catalysts

Supported catalysts were prepared by the impregnation method. 1.0 g of a support was added to a solution of $Ru(acac)_3$ (79.5 mg, 0.20 mmol) in 10 mL of THF in air at room temperature. After impregnation, the resulting powder was calcined in air at 400 ^{o}C for 30 min to afford the Ru(2.0 wt%)/Support catalyst.

8.4.4 General procedure for the hydroacylation of alkynes by Ru/CeO_2 catalysts

2,6-Dimethylbenzaldehyde **1l** (67 mg, 0.50 mmol), diphenylacetylene **2a** (267 mg, 1.5 mmol), sodium formate (10.2 mg, 0.15 mmol), Xantphos (28.9 mg, 0.050 mmol) and *N*,*N*-dimethylacetamide (2.0 mL) were placed in a glass Schlenk tube under an argon atmosphere together with 125 mg of Ru/CeO_2 (0.025 mmol as Ru). The reaction mixture was stirred at 150 ^{o}C for 5 h on a hot stirrer equipped with a cooling block. After the reaction, the solution was separated from the reaction mixture by centrifugation and concentrated under reduced pressure. The products were isolated by a

column chromatography (hexane : ethyl acetate = 20:1, v/v) to give the product **3l** as a white solid; yield: 146 mg (86%).

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[9] Abbreviations: dppe, 1,2-bis(diphenylphosphino)ethane; dppb, 1,4-bis(diphenylphosphino)butane; dpppe, 1,5-bis(diphenylphosphino)pentane; dppf, 1,1'-bis(diphenylphosphino)ferrocene; *rac*-BINAP, racemic-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl; DPEphos, bis[(2-diphenylphosphino)phenyl] ether; ^{t}Bu-Xantphos, 4,5-bis(di-*tert*-butylphosphino)-9,9-dimethylxanthene.

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General Conclusion

In this thesis, the development of supported Ru catalysts effective for various organic synthetic reactions is described. The general outline of this thesis is as follows; In chapter 1, sequential transfer-allylation–isomerizaiton of homoallyl alcohols to aldehydes by a heterogeneous Ru catalyst was examined. The reaction took place in the presence of Ru/CeO_2 catalysts to give saturated ketones in good to high yields. The reaction did not require any additives such as bases, phosphines, or CO. The solid Ru catalysts worked heterogeneously and could be recycled several times without a loss of activity. In contrast, the Ru catalysts supported on SiO_2, Al_2O_3, TiO_2 or MgO did not show any activities.

In chapter 2, the direct arylation of aromatic C–H bonds with aryl halides in the presence of oxide-supported Ru catalysts was described. Ru/CeO_2 and Ru/ZrO_2 showed activities for the reaction to afford the corresponding unsymmetrical biaryl compounds in high yields. Furthermore, pretreatment of Ru/CeO_2 in the presence of PPh_3 under a hydrogen atmosphere markedly increased its catalytic activity. The reaction of aromatic C–H bond with various aryl chlorides in the presence of the PPh_3-modified Ru/CeO_2 catalysts (PPh_3–Ru/CeO_2) proceeded efficiently to give the products in excellent yields. Successful recycling of the solid Ru/CeO_2 catalysts was also demonstrated.

In chapter 3, the catalytic addition of aromatic C–H bonds to vinylsilanes in the presence of supported Ru catalysts was examined. The reaction occurred in the presence of Ru/CeO_2 together with a catalytic amount of PPh_3. Moreover, PPh_3-modified Ru/CeO_2 catalysts showed very high activities. However, the recycling of the Ru/CeO_2 catalysts

were not realized due to the irreversible deposition by siliceous compounds on the surface Ru species, and the catalytic system were not effective for the reaction of alkenes other than alkoxyvinylsilanes.

In chapter 4, the hydroarylation of various alkenes in the presence of Ru/CeO_2 catalysts was reported. The treatment of Ru/CeO_2 with PPh_3 and HCHO in 2-methoxyethanol was found to generate highly active Ru catalysts for the hydroarylation of various unsaturated compounds. The solid Ru catalysts could be recycled several times without a significant loss of activity.

In chapter 5, the addition of carboxylic acids to terminal alkynes by solid oxide-supported Ru catalysts was examined. Ru/CeO_2 and Ru/ZrO_2 catalysts showed activities for the reaction to give the corresponding vinyl esters in high yields. In the present catalytic system, *E*-isomer of anti-Markovnikov adducts were obtained as the major products and the solid Ru/CeO_2 catalysts could be recycled for several times without a significant loss of activity.

Chapter 6 described the preparation of active Ru catalysts from Ru/CeO_2 by phosphine-modification, which were effective for the regio- and stereo-selective addition of carboxylic acids to terminal alkynes. Ru/CeO_2 catalysts modified by dppb under a hydrogen atmosphere gave *Z*-isomers of anti-Markovnikov adducts in high yields with excellent selectivities. In contrast, Ru/CeO_2 catalysts modified by $P(^nOct)_3$ were effective for the selective production of Markovnikov adducts.

In chapter 7, the intermolecular coupling of alkynes with acrylates in the presence of supported Ru catalysts was described. Ru/CeO_2 and Ru/ZrO_2 showed high catalytic activities for the reactions in the presence of a catalytic amount of sodium formate. Detailed spectroscopic analyses indicated that the formation of distorted Ru(IV)-oxo

species on CeO_2 and ZrO_2, which was transformed into catalytically active low-valent Ru species at the initial stage of the reaction. The solid Ru catalysts could be applied for the reaction with both of internal and terminal alkynes and could be recycled without a loss of activity. Furthermore, the cross coupling reaction of two different alkenes was also realized by this catalytic system.

Chapter 8 described the intermolecular hydroacylation of alkynes by recyclable Ru catalysts. Ru/CeO_2 catalyst showed activity toward the reaction in the presence of sodium formate and Xantphos to give the corresponding conjugated enones in moderate to high yields. Various aromatic aldehydes with or without coordinating groups could be used for the reactions. The solid Ru/CeO_2 catalysts could be recycled for several times without a significant loss of activity.

In summary, Ru/CeO_2 and Ru/ZrO_2 catalysts are found to show high catalytic performance for various organic synthetic reactions. As described in this thesis, the present catalytic systems have excellent environmentally-compatibility due to their high recyclability and low contamination of the products by metallic species. The most characteristic feature of the Ru/CeO_2 and Ru/ZrO_2 catalysts is the formation of Ru(IV)-oxo species on CeO_2 and ZrO_2, which were not observed in SiO_2-, Al_2O_3-, TiO_2- and MgO-supported Ru catalysts. Under appropriate conditions, such special Ru-oxo species can be transformed into catalytically active Ru species effective for various synthetic reactions. The present catalysis is completely different from classical oxide-based catalysts and supported Ru catalysts in terms of their diversity of applicable reactions. These new findings will contribute to the progress of green-sustainable organic synthesis.

List of Publications

Chapter 1

"A heterogeneous Ru/CeO_2 catalyst effective for transfer-allylation from homoallyl alcohols to aldehydes"

Hiroki Miura, Kenji Wada, Saburo Hosokawa, Masahiro Sai, Teruyuki Kondo, Masashi Inoue

Chem. Commun., **2009**, 4114–4114.

[*Highlighted in Synfacts*, **2009**, 1174], [*Highlighted in ChemInform*, **2009**, *40*, 46]

Chapter 2

"Recyclable solid ruthenium catalysts for the direct arylation of aromatic C–H bonds"

Hiroki Miura, Kenji Wada, Saburo Hosokawa, Masashi Inoue,

Chem. Eur. J., **2010**, *16*, 4186–4189.

[*Highlighted in Synfacts*, **2010**, 847], [*Highlighted in ChemInform*, **2010**, *41*, 35]

Chapter 3

"Catalytic addition of aromatic C–H bonds to vinylsilanes in the presence of Ru/CeO_2"

Hiroki Miura, Kenji Wada, Saburo Hosokawa, Masashi Inoue,

ChemCatChem, **2010**, *2*, 1223–1225.

Chapter 4

"Transformation of ruthenium(IV)-oxo species on CeO_2 to active ruthenium catalysts for the addition of aromatic C–H bonds to unsaturated compounds"

Hiroki Miura, Masahiro Nagao, Kenji Wada, Saburo Hosokawa, Masashi Inoue,

Manuscript under preparation.

Chapter 5

"Recyclable solid ruthenium catalysts supported on metal oxides for the addition of carboxylic acids to terminal alkynes"

Masami Nishiumi, Hiroki Miura, Kenji Wada, Saburo Hosokawa, Masashi Inoue

Adv. Synth. Catal., **2010**, *352,* 3045–3052.

Chapter 6

"Selective addition of carboxylic acids to alkynes in the presence of recyclable ruthenium catalysts prepared through phosphine-modification of ruthenium(IV) species supported on ceria"

Masami Nishiumi, Hiroki Miura, Kenji Wada, Saburo Hosokawa, Masashi Inoue

Submitted for publication.

Chapter 7

"Intermolecular coupling of alkynes with acrylates by recyclable oxide-supported ruthenium catalysts: Formation of distorted ruthenium(IV)-oxo species on ceria as a key precursor of active species"

Hiroki Miura, Shun Shimura, Saburo Hosokawa, Seiji Yamazoe, Kenji Wada,

Masashi Inoue

Adv. Synth. Catal., **2011**, *353*, 2837–2843.

[*Highlighted in Synfacts*, **2012**, 111]

Chapter 8

"Intermolecular hydroacylation of alkynes in the presence of recyclable Ru/CeO_2 catalysts"

Hiroki Miura, Kenji Wada, Saburo Hosokawa, Masashi Inoue

Manuscript under preparation.

Papers not included in this thesis

"Ceria-supported ruthenium catalysts for the synthesis of indole *via* dehydrogenative *N*-heterocyclization"

Shun Shimura, Hiroki Miura, Kenji Wada, Saburo Hosokawa, Seiji Yamazoe,

Masashi Inoue

Catal. Sci. Technol., **2011**, *1*, 1340–1346.

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